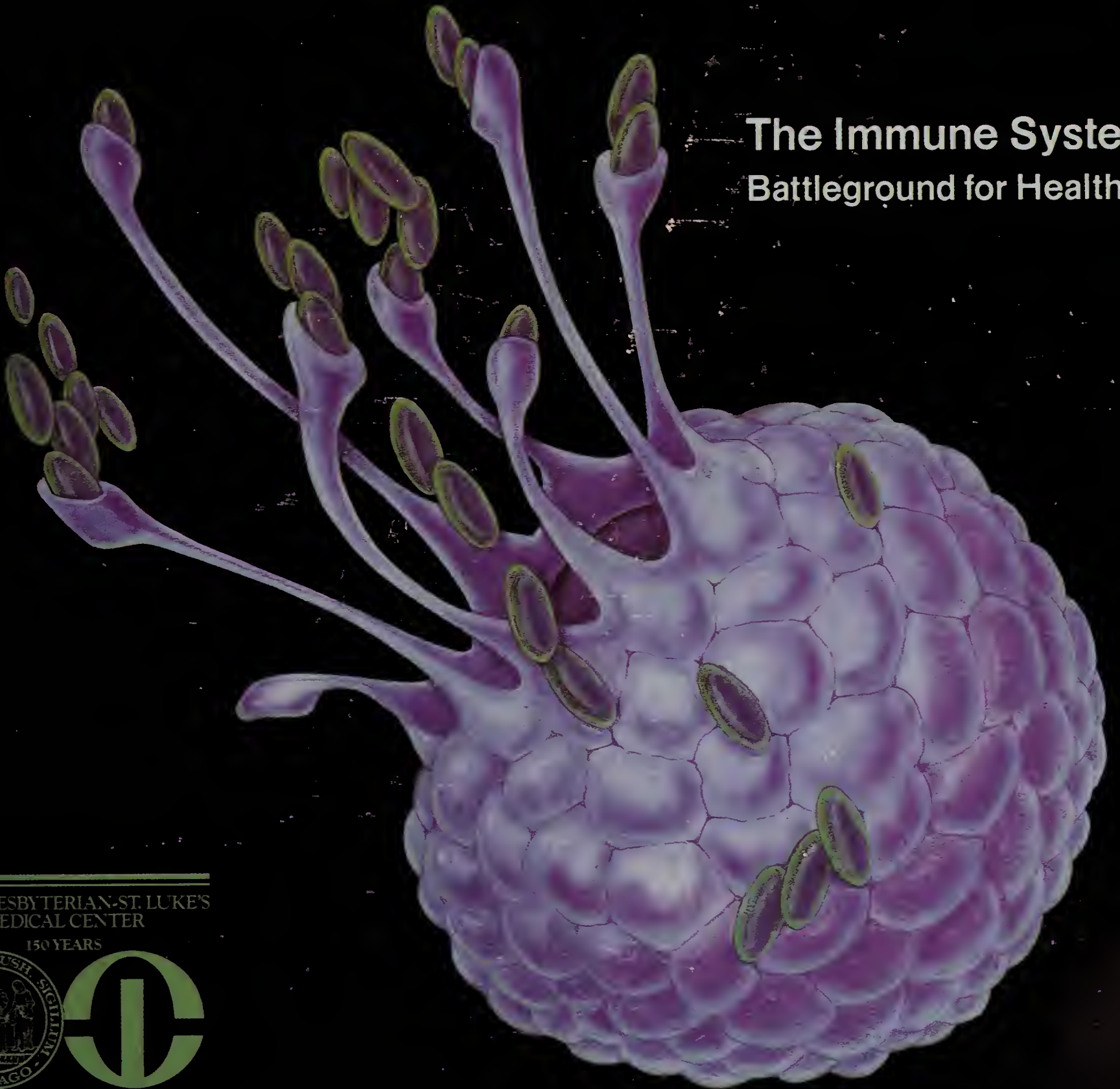


RUSH-PRESBYTERIAN-ST. LUKE'S MEDICAL CENTER

The Magazine

Winter 1986-87

**The Immune System
Battleground for Health**



RUSH-PRESBYTERIAN-ST. LUKE'S
MEDICAL CENTER

150 YEARS



1837 1987
A Chicago Tradition A National Resource

**Medical Center
observes Sesquicentennial**

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A Chicago Tradition/A National Resource



The beginning: Rush Medical College's first building, 1844.



The Medical Center today.

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More than a century and a half ago, an intrepid pioneer physician/surgeon rode into the village of Chicago on his pony, after an arduous overland trip from his New York state home. His intention was to set up his practice in this growing frontier area. This he did almost at once—but he also did much more for the health and well-being of Chicago citizens down to the present day. In 1837, Dr. Daniel Brainard obtained a charter for Chicago's first medical school and named it for Benjamin Rush, the only medical doctor to sign the Declaration of Independence. In doing so he launched a tradition of health education, care and research which continues today at Rush-Presbyterian-St. Luke's Medical Center.

The three institutions represented in the name of today's modern academic medical center were all founded before the turn of the 20th Century, in a city just beginning to progress from frontier town to major American metropolis. These institutions—Rush Medical College, Presbyterian Hospital and St. Luke's Hospital—and the City of Chicago have all grown together.

Rush Medical College

Rush Medical College was chartered on March 2, 1837, just two days before the city of Chicago was incorporated. The first students, however, did not begin classes until 1843, the opening postponed in part by the Panic of 1837 and the founder's study in Europe. Just 22 students were in this first class, but 50 years later, Rush was the largest medical school in the United States with 850 students and 80 teachers. Its first faculty members included physicians whose names have gone down in the annals of medical progress.

In its early years, Rush was a free-standing medical school, like others of its time. However, unlike many of its fellows, Rush, early on, sought affiliation with an institution of higher learning—a goal reflecting the early faculty's penchant for providing academic as well as clinical experience. Its first affiliation with Lake Forest College lasted from 1887 to 1898. Next, Rush affiliated with The University of Chicago, a union in effect from 1898 to 1941. This union saw a reorganization of the Rush curriculum, with the first two years devoted to pure science, and a growing emphasis placed on post-graduate medical education and research. Indeed, when the Flexner Report on medical education was released in the early 1900s, Rush Medical College's curriculum was cited as an example for others to follow.

After 1941, the Rush faculty became part of the faculty of the University of Illinois, and Rush Medical College, for a time, existed only in its charter, kept in effect by a band of devoted alumni and faculty. This academic hiatus ended in 1969 when Rush Medical College joined with two respected hospitals—Presby-

terian and St. Luke's which had already merged—to form the present day medical center.

St. Luke's Hospital/Presbyterian Hospital

♦ St. Luke's Hospital, established in 1864, was a response by the pastor and the Ladies Aid Society of Grace Episcopal church for "a clean, free Christian place where the sick poor might be cared for." It opened in a refurbished private house with just seven beds. By 1871 it had moved location and increased bed size to 25—setting a pattern of movement and growth that was to characterize its beginnings. Many of the early staff at St. Luke's were Rush professors, establishing early on the relationship between the two institutions.

In 1883, following a move to yet another newer and larger facility, St. Luke's opened a training school for nurses—only the 35th in the United States—organized on the Florence Nightingale model, with the training supervised by nurses, not doctors.

Always innovative, the St. Luke's staff made the hospital the site of many medical "firsts." The first heart surgery, performed by Dr. Daniel Hale Williams, reportedly took place at St. Luke's, as did the first Caesarean section in the midwest and the first use of hypnosis as an anesthetic during surgery.

♦ Presbyterian Hospital has been affiliated with Rush Medical College since its beginnings. In 1879, Rush bought land on which to build a hospital. The venture proved to be too much of a challenge for the school's budget, so members of the city's Presbyterian churches took on the responsibility, establishing the new hospital

in 1883 with 80 beds. Presbyterian, staffed by Rush faculty members, served as a site for Rush Medical College's clinical programs and research efforts. Presbyterian, too, established a school of nursing; this school, together with the St. Luke's school of nursing, were worthy predecessors of today's Rush University College of Nursing.

The institution also had its share of innovative programs contributing to the advancement of health care. In the early 1950s, for example, surgical experimentation on organ transplantation was underway. It was also the site of the city's first heart catheterization, performed—fittingly enough—in the hospital's new cardiac catheterization lab, also a Chicago first.

In 1956, these two pioneering institutions merged. St. Luke's, born and raised on Chicago's near south side, moved to the near west side, joining Presbyterian within the West Side Medical Center, said to be the largest concentration of health care facilities in the world.

Rush-Presbyterian-St. Luke's Medical Center

Rush-Presbyterian-St. Luke's Medical Center came into being in 1969, when a reactivated Rush Medical college was joined with Presbyterian-St. Luke's Hospital. This new entity, an academic medical center, brought together patient care, education and research in the health fields.

Today, 150 years after Dr. Daniel Brainard chartered his medical college and almost two decades after these respected Chicago institutions merged their traditions, Rush-Presbyterian-St. Luke's ranks among the major medical centers of the nation. Each of its components has grown in size and stature.

♦ Rush Medical College is now one of the four colleges of Rush University, a health professions institution enrolling more than 1,100 students in its colleges of medicine, nursing, health sciences and graduate studies. The University has awarded more than 3,600 undergraduate and graduate degrees since 1972. It has 33 endowed chairs and an academic facility providing the most modern classroom, laboratory and learning resources.

♦ Presbyterian-St. Luke's Hospital, a tertiary care hospital providing highly sophisticated treatment for seriously ill patients, has been joined by the Johnston R. Bowman Health Center for the Elderly, one of the country's outstanding geriatric treatment centers, and Sheridan Road Hospital, a community based care center.

Together, these three institutions cared for more than

32,000 inpatients during the past year.

♦ More than \$13 million in awards currently support the Medical Center's 1,223 active research projects. These projects have resulted in over 1,000 publications through which their findings are shared with others concerned with new knowledge that can lead to improved treatment and better health. Major areas of study are cancer, heart disease and neurological diseases.

The Medical Center is also a leader in developing new modes of health care delivery, in response to our nation's changing health care climate. Its ANCHOR Organization for health maintenance—a pioneer of its type now 15 years old—is one of the country's most successful HMOs with over 130,000 members and 18 office locations in Illinois and Indiana. Recent additions to Rush services include ACCESS Health, an independent practice association model health maintenance organization; Rush Contract Care, a preferred provider organization; the Rush Occupational Health Network, serving over 3,000 employers in six locations in Chicago and suburbs; Rush Home Health, offering specialized care in the home, and several satellite offices.

The Medical Center's continuing quest for quality patient care is reflected in the advanced diagnostic and treatment technology available within its many specialized departments, as befits an institution where half the medical-surgical beds are for patients referred from other institutions because of the seriousness or complexity of their illness. Recent acquisitions include magnetic resonance imaging and a lithotripter for pulverizing kidney stones with shock waves.

In this sesquicentennial year, the Medical Center is taking the time to look back at its heritage with pride. It is also looking ahead to the future, planning for tomorrow's health needs in ways that will continue the tradition of excellence it has always espoused and which has contributed effectively for a century and a half to the health and well-being of the society it serves.



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Cover: A macrophage, an "immune system soldier," devouring microorganisms foreign to the body.

The Immune System: Battleground for Health

By Krys Kazieczko-Kuszek
Janice Perrone
Kris Hansen

You're not feeling well. Muscles ache. Stomach feels queasy. And the thermometer shows a slight temperature. It's nothing serious, though. A little rest over the weekend and, by Monday, you're back on your feet.

Your immune system has won another battle to keep your body healthy.

The actual struggle to stay healthy is complicated. The immune system involves hundreds of thousands of tiny cells throughout the body tissues and in the bloodstream. All are initially formed in the bone marrow but organs like the thymus, spleen and lymph nodes also have important roles in the body's built-in mechanism for self-defense.

Exactly how this system works is still not completely understood. However, immunology study and

research, particularly in recent years, have put more and more pieces of this intricate puzzle into place.

Immunology is a new science, even though its earliest discoveries date back some 200 years. It was then that English physician Edward Jenner found that a vaccine against cowpox, a relatively mild disease, protected his patients against the dreaded smallpox.

But the pace of discovery was slow at first.

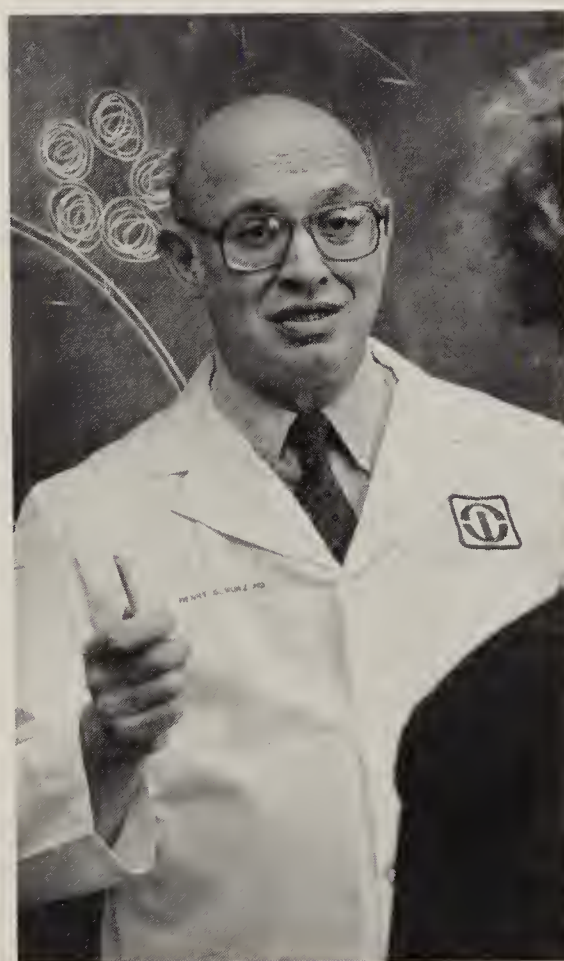
Not until the mid-1800s was it recognized that microbes cause disease, a discovery by Louis Pasteur. At the turn of the century, Russian biologist Eli Metchnikoff noticed that certain blood cells surround and destroy invading disease-causing bacteria.

"The field of immunology has exploded since then," says Henry Gewurz, M.D., the Thomas Coogan, Sr., M.D., professor and chairman of the Department of Immunology/Microbiology at Rush-Presbyterian-St. Luke's Medical Center.

It was an explosion linked to developments of these times.

"Much of what we know about the immune system only became possible in this age of organ transplantation and sophisticated cancer therapy," explains Dr. Gewurz. One of the most influential factors was the recent outbreak of AIDS, the fatal autoimmune deficiency syndrome, which has spurred research by immunologists around the country.

"Today," adds Dr. Gewurz, "immunology is truly appreciated as a key



Henry Gewurz, M.D., is an authority on changes during the acute phase of illness, when inflammation and tissue damage are at their peak.

Thomas F. Lint, Ph.D., studies complement proteins in the blood to determine their exact role in protecting the body.

to understanding—and overcoming—illness and disease.”

Battling Bacteria and Viruses

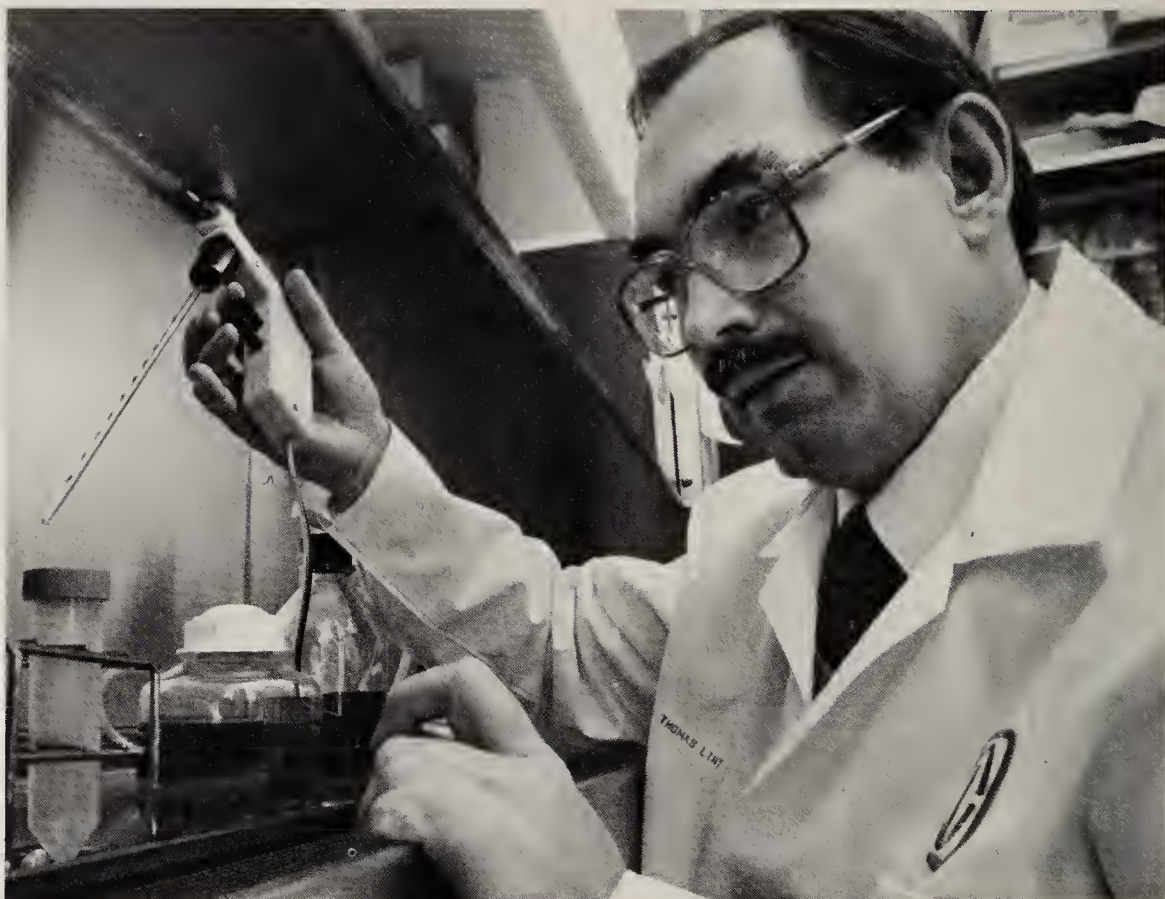
A simple finger cut. Nothing to worry about. But then bacteria get in. How do you defend yourself? Can that bacteria overwhelm you? Can the infection kill you?

“If you didn’t have an immune system, the answer would be yes,” says Thomas F. Lint, Ph.D., associate professor of immunology/microbiology at Rush Medical College.

He details what happens:

As bacteria start to grow at the cut, some fragments move into the lymph, the fluid that bathes all of your tissues. Eventually bacteria get to one of the lymph nodes. Located throughout your body, lymph nodes are factories for the immune system where macrophages, T-cells and B-cells all cooperate in the production of antibodies.

A macrophage is a scavenger cell that circulates in the bloodstream as well as the body’s tissues. Its name, translated from the Greek, means “big eater,” which aptly describes its job when it comes in contact with any microorganism that is not part of the body. But at this point the macrophage is not a very efficient worker, Dr. Lint says. There are also some bacteria that are very resistant to these cell-eaters so other immune system soldiers need to be called into play. These are the white blood cells called lymphocytes, specifically T-lymphocytes (also known as T-cells) and B-lymphocytes (B-cells).



A lymphocyte answers only one call to battle—an antigen. An antigen is that part of a microorganism that marks it as foreign and generates an antibody response. Bacteria naturally shed or leak these antigens which are picked up by scavenger macrophages.

After the antigen of the bacteria from the finger cut is taken up by a macrophage, the macrophage continues bumping into T-cells and B-cells, all the while displaying the antigen like a sign.

Each T-cell and B-cell is programmed to recognize just one particular antigen. The B-cell, however, depends on a “helper” T-cell to get activated. Like a pinball in an arcade game, a macrophage may bump into thousands of different lymphocytes, but nothing happens until it meets a T-cell that recognizes the antigen of the bacteria and sounds the alarm to trigger the

antibody response.

This helper T-cell signals the proper B-cell which, in turn, transforms itself into a plasma cell that custom-builds antibody for the specific invader. The antibody goes into the blood, making its way back to the target bacteria.

When antibody tackles and attaches to the bacteria, that antibody activates complement proteins that make the antigens more vulnerable to attack. Little fragments released from complement proteins call in the macrophages.

“Complement is like honey on the surface of the bacteria,” Dr. Lint explains. It attracts macrophages and makes them super efficient in digesting and metabolizing the bacteria. This process of eliminating invading cells by ingestion is known as phagocytosis and also includes other “cell eaters” (phagocytes) called neutrophils. As the battle is

"Much of what we know about the immune system only became possible in this age of organ transplantation and sophisticated cancer therapy."

Henry Gewurz, M.D.

won, suppressor T-cells start their job of slowing down the immune response.

Dr. Lint compares the body's immune system to a component stereo system and likens the invading bacteria to a record album.

"The needle is like antibody," he explains. "It recognizes the grooves on the record, but that alone is insufficient to produce music. The information picked up by the needle is transferred to an amplifier; amplification is one of the jobs of the complement system. To get the best sound on your stereo, you might need to adjust the treble or the bass. That kind of fine-tuning is what the T-lymphocytes do; helper T-cells and suppressor T-cells carry out the job of controlling the antibody response."

But even with all those components, you do not hear music if the effector, the speaker system, is missing. In immunology, there is more than one kind of effector system to carry out the final job of destroying and eliminating the invader. Which system gets activated depends on the enemy.

With bacteria, antibody and phagocytosis come into play. But viruses call for special tactics, Dr. Lint explains.

A virus actually enters a body cell and takes it over. The only way to eliminate this virus, therefore, is to destroy the cell that has the virus in it. Two different kinds of immune system soldiers have that role—killer T-cells and natural killer cells.

Killer T-cells depend on helper T-cells to get triggered into action. Natural killer cells, on constant patrol throughout the body, are lone bounty hunters that act independently to eliminate certain virus infections and cancer cells.

Study of what Dr. Lint calls the

immune system's "amplification" and "effector" mechanisms has been a primary focus of research at the Medical Center.

"We are purifying complement proteins from the blood, analyzing their structure and genetics and trying to find out their exact role in protecting the body against foreign molecules," Dr. Lint explains.

There are at least 23 different complement proteins. In very rare instances, a person might lack one of the complement components. This is sometimes the case with patients who have autoimmune diseases such as systemic lupus erythematosus. Complement deficiency has also been linked to recurrent infections, especially meningitis or gonorrhea.

Medical Center laboratories have identified more patients with inherited complement deficiencies than any other in the world.

"This has proven to be extremely useful in determining the role of complement in defending the body," Dr. Lint says. "By studying patients with deficiencies and seeing how their immune systems fail, we can extrapolate and determine what the particular missing complement protein normally does."

Complement proteins are identified as C1 through C9 and each seems to have a very specific role.

The protein C5a, for example, makes white blood cells gather together in a specific area to fight invading pathogens.

Immunologists know that C5b triggers the assembly of proteins C6, C7, C8 and C9 into a giant macromolecular complex which Dr. Lint describes as looking like a donut, but acting like a fighter—actually punching holes into bacterial cell membranes and killing

them. This particular combination of proteins is called the complement attack complex and is of special research interest to Dr. Lint and his colleagues.

Rush researchers were the first in the world to discover a patient with a C9 deficiency and are continuing study of the biochemistry of this complement deficiency.

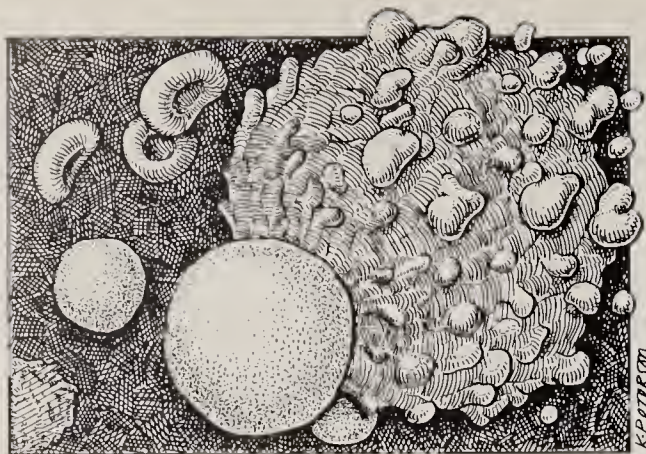
They have also developed monoclonal antibodies to target different subcomponents of complement attack molecules. By tracking these antibodies that have been cloned in the laboratory, researchers are able to probe just how complement attack molecules assemble to destroy bacteria cells.

Activation of the attack complex of complement is also being measured by an extremely sensitive test devised by Maria Gawryl, Ph.D., assistant professor of immunology/microbiology.

"This may turn out to be one of the most important things we have done," says Dr. Lint, "because it may allow us to use clinical measurements of complement activation to assess disease level activity in patients."

Complement gets activated in many different diseases, so that alone is not indicative of any given illness. However, Drs. Lint, Gawryl, and colleagues are suggesting that the degree of complement activation may indicate how active the disease process is in a patient. "We're finding that this is indeed the case in some autoimmune diseases including systemic lupus erythematosus.

"By using our new test to measure complement activation," Dr. Lint adds, "we can better assess how well the patient is doing on therapy and help the physician fine tune the degree of anti-inflammatory



A large cancer cell being attacked by a T-cell.

drugs necessary to keep the disease in check."

Preliminary studies also seem to indicate that this new test can be used to determine how far along the inflammation has progressed.

"This has a lot of exciting potential, but we're just beginning to study the disease associations," Dr. Lint cautions.

"We've spent a lot of time in the past years doing basic biochemistry. Now we're ready to take what we've discovered and developed in the research laboratory and begin applying it to clinical situations."

Tracking Illness and Recovery

What happens when you first get sick?

Fever is often one of the earliest symptoms of the acute phase of illness, when inflammation and tissue damage are at their peak. High pulse rate is another. Blood also changes. Together, these initial body reactions to sickness or injury are known as the acute phase response.

Acute phase response has been a special focus of investigation by Dr. Gewurz and his colleagues, recognized worldwide for their studies of the blood protein called C-Reactive Protein (CRP).

Of all the acute phase proteins found in the blood, CRP is the most noticeable.

Normal serum has just trace amounts of CRP. With inflammation or tissue damage, however, CRP levels soar. They rise precipitously within hours of surgery, for example, during bouts of rheumatoid arthritis and when infection sets in. In some cases the amount of CRP increases by as much as a thousand times.

Because CRP changes are non-

specific, they can't be used for diagnosis, Dr. Gewurz says, "but they do provide a good clinical barometer of illness.

"We can measure CRP levels in blood samples to screen patients for sickness, monitor effectiveness of therapy and chart the progress of recovery," he explains.

Rush researchers are now looking at the functional activities of CRP. "What we're seeing in the laboratory is a fairly broad picture of its potential biological role," says Dr. Gewurz.

In the past decade it has become clear that CRP is similar to antibody in many ways. It recognizes certain foreign substances and, like antibody, targets them to be cleared away from the body.

Studies by Janice Zeller, Ph.D., R.N., assistant professor of immunology/microbiology and associate professor of medical nursing, suggest that CRP might also assist antibody.

She explains that when tissues first become inflamed and levels of antibody in circulation are very low, CRP seems to act with the antibody to trigger the fighting white blood cells programmed to swallow up invading bacteria.

Researchers have also found that CRP appears to provide protection against certain bacterial infections in laboratory animals. Those findings are preliminary, Dr. Zeller cautions, "but in the future we may be able to give patients who can't develop their own high level of CRP a purified dose to help their white blood cells fight infection and disease."

"Of all the acute phase proteins," adds Dr. Gewurz, "we know the most about CRP, but many questions remain about what this protein does and how it does it."

Continued research to find the answers has called attention to the other blood proteins that also change in concentration during inflammation.

"At first, all these changes were thought of simply as a reflection of illness or injury—like footprints," Dr. Gewurz explains.

"Now we're finding more and more evidence to suggest that acute phase proteins have a key role in the body's fight to stay healthy."

This struggle to maintain health was originally thought to be strictly a battle against invaders—harmful bacteria and disease-causing viruses. But, in recent years, much has been discovered about the immune system.

Today we know that it defends against disturbances from within, playing a key role in the body's surveillance against cancer. In AIDS, the immune system shuts down. In allergies it starts up without need. In organ transplantation it becomes a threat.

Cancer. AIDS. Organ transplantation. Allergies. Each of these areas is a focus of research by immunologists at the Medical Center.

K.K.-K.

"We've been trying to understand how cancer causes an immune deficiency and how anti-cancer therapies might be designed to circumvent or even eliminate that situation."

Donald Braun, Ph.D.

Cancer: An Ancient Enemy

Cancer is one of the immune system's oldest enemies—and one of the most formidable. For millions of years it's been battling with its victims, usually winning. Birds, dogs, plants, and, of course, man...it seems to afflict all living things. Scientists have found evidence of cancer in dinosaur bones and in 5000-year-old Egyptian mummies; ancient medical writings name the disease, define its symptoms, and note its bleak prognosis.

Since the invention of microscopes in the 1800s, scientists have learned a lot about cancer and how a tumor grows, but in many cases the prognosis today is just as bleak as it ever was. Last year 462,000 Americans died of cancer; this year another 930,000 will be told they have the disease, and, without significant treatment advances, more than half of them will die in the next five years.

Why does cancer occur? And how are researchers today fighting alongside the immune system to stop it?

"A tumor is thought to result from an alteration in the DNA of a cell," says Donald Braun, Ph.D., assistant professor of immunology/microbiology.

It's a case of cells trying to revolt, to grow unbridled; a mutiny against the body's rigid rules.

The second step in the ominous

sequence that can result in cancer is the creation of an environment that permits these clones to grow. "It's in this environment that the immune system first steps in to fight back," notes Dr. Braun. "The system recognizes an enemy and is activated to try to eliminate these new malignant clones."

Scientists think that these malignant clones develop in our bodies all the time, but that the immune system is usually able to wipe them out long before they can form a visible tumor.

"Once the system has been activated, it's capable of discriminating between normal and malignant tis-

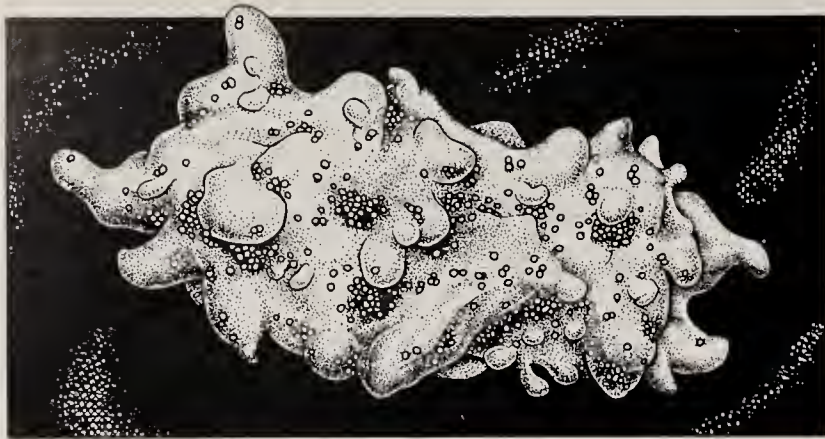
sue," continues Dr. Braun. "But malignant tissue looks very similar to normal tissue, and cancer cells are particularly adept at trying to circumvent the immune system by masking or shedding their antigens, or producing substances that weaken the immune system. So this subclinical, subdetectable process is really the battleground for a war against a cancer."

It's at this point that the tumor is stopped dead in its tracks. It is not allowed to grow and kill the host. The malignant cells lose, the body wins...when the immune system is working right.

"There are several things that



Donald Braun, Ph.D., is testing ways to improve immune responses in cancer patients.



The helper T-cell is the target of the AIDS virus (small dots). When helper T-cells are destroyed, the immune system shuts down.

can tip the balance in favor of the malignant cells," says Dr. Braun.

These include immunosuppressive drugs like those given to transplant patients; long-term steroid therapy, necessary for a variety of medical conditions; anything else that depresses the immune system, like poor nutrition; or just the aging process.

When these things overwhelm the immune system, the body starts to lose, and a tumor becomes clinically obvious.

The immune system may be down, but it's not yet out.

"Before the tumor becomes visible, natural killer cells and macrophages are working to eliminate it," notes Dr. Braun. "After a tumor develops, there are other cells in the immune system, T-cells, that become activated to try to control it. It's unlikely that the immune system can, all by itself, eliminate a tumor once the tumor is clinically obvious. But it can still play a role in controlling the rate of tumor growth and in contributing to the eventual elimination of tumor cells—if other interventions like surgery, radiation, or chemotherapy are applied."

This points out one of the dilemmas in cancer care. Many therapies used to treat a malignancy also suppress the immune system, so that while they may be eliminating tumor cells directly, they may be indirectly interfering with the ability of the immune system to do its job.

"The problem of immune deficiency in cancer patients has really been our major area of research," says Dr. Braun. "We've been trying to understand how cancer causes an immune deficiency and how anti-cancer therapies might be designed to circumvent or even eliminate that situation."

One such study is a National

Cancer Institute-funded trial of Interleukin II, a growth factor for the immune system.

"The rationale here is that the immune deficiency we see in cancer patients might be overcome if we provide the system with growth factors that improve immune responses," notes Dr. Braun. For this study, researchers will be working with colon cancer patients who have a high likelihood of having the cancer recur. "Sometimes malignant cells are left behind after surgery or other kinds of anti-cancer therapy, but not enough for us to detect them clinically and do something about them," Dr. Braun says. "We hope that having a more competent immune system will permit patients to resist the reemergence of the tumor."

Another way to augment the immune system, and the one that's currently generating the most interest among researchers, is through manipulating prostaglandins, substances that have many biological roles but whose effect, generally, is to shut off immune responses. One of the major findings from Dr. Braun's lab is that cancer patients produce too many prostaglandins.

"We have shown in the lab that we can stop this excessive prostaglandin production in cancer patients," says Dr. Braun, "and by doing so restore normal immune responses."

This excessive production of prostaglandins occurs in a cancer patient's monocytes, cells that develop into macrophages, the scavengers in the immune system that surround and digest invaders.

To date, the restoration of normal immune responses in the monocytes of cancer patients has been accomplished in patients who are very ill, whose clinical status is

considered end-stage. "So we can't say that improving their immune system improved their condition," says Dr. Braun. "But we speculate that restoring immune responses might be beneficial to a patient whose disease is not as advanced."

A new study recently began at Rush to test this theory. Researchers are working to upgrade the immune systems of patients who have limited amounts of head and neck cancer, but who already have drastically reduced immune function. The two-year study involves an anti-arthritis drug called piroxicam, which stops prostaglandin production.

"We're also participating in a number of studies with the drug interferon. We plan to combine it with piroxicam to try to augment the immune systems of patients with renal cell cancers," notes Dr. Braun. "And, once again, the reason for this is to try to improve the function of their immune system by stopping abnormal monocyte suppression."

This tiny monocyte, a single cell running through your bloodstream, may not only be the key to improved cancer care, but also to a breakthrough in another major immune system disorder, AIDS.

"Aids infects the immune system through the T-4 lymphocyte. These cells are critical for the body to mount an effective response against an invader. The virus, in effect, wipes out the conductor of the orchestra and the rest of the players don't know what to do."

Alan L. Landay, Ph.D.

AIDS: A New Adversary

If cancer is one of the immune system's oldest enemies, AIDS is one of the newest.

It seemed to come out of nowhere in 1981. A disease that struck homosexuals, primarily. It caused rare cancers in otherwise healthy young men. It was invariably deadly, usually within a few years.

No one can be sure where AIDS came from, but most scientists believe the story starts with a monkey in Central Africa. The monkey, they believe, had harbored a harmless version of the AIDS virus in its bloodstream. Then, through some kind of random, genetic mutation, the virus took on a deadly character. Like other viruses, it crossed over from animals to humans. And it spread.

"We've known for several years that when the AIDS virus comes in contact with man, it infects the immune system through the lymphocyte known as the T-4 lymphocyte," says Alan L. Landay, Ph.D., assistant professor of immunology/microbiology and director of the Clinical Immunology Laboratory and Flow Cytometry Facility.

"These cells are critical for the body to mount an effective response against an invader. They coordinate the rest of the cells in the immune system. That's why AIDS is so deadly. The virus, in effect, wipes out the conductor of the orchestra and the rest of the players don't know what to do."

But in just the last few months, Dr. Landay says, scientists have made another important discovery about the infection process. Before it infects the lymphocytes, the virus, now known as human immunodeficiency virus (HIV), apparently infects monocytes and macrophages.

"We know that when HIV infects a T-cell, it kills the cell," says Dr. Landay. "When the virus enters the monocyte, it probably does not kill the monocyte, but may affect some of its functions."

These effects of the AIDS virus on monocyte function may have

important implications for predicting which people at risk for getting AIDS will go on to develop it.

Dr. Landay explains that when someone is exposed to AIDS, he may become sick with an illness like mononucleosis, get over it, and be healthy for a long time. "He's sort of sitting there like a loaded gun waiting for the trigger to be pulled," Dr. Landay says. "Usually, some secondary event comes along to pull that trigger, and the person gets AIDS. What that secondary event is is under active investigation."



Immunologists Harold A. Kessler, M.D., and Alan L. Landay Ph.D., combine research efforts in the fight against AIDS.

Some probable secondary events include being exposed to certain recreational drugs; some blood products; sperm, which may stimulate the immune system and bring out the latent form of the virus; and other viruses, like herpes and hepatitis.

Because of their lifestyles or medical conditions, homosexuals, drug users, and hemophiliacs are in the risk groups for AIDS. And the time from their exposure to the virus to development of the disease seems to be as much as five years.

"We'd like to be able to give these people, who are currently healthy but very scared, some information," says Dr. Landay. "What are their chances of getting AIDS? How often should they see their doctor? Can anything be done to prevent them from ever getting AIDS? This is where we want to focus our efforts at Rush."

To answer these questions, a multidisciplinary team is studying monocyte and macrophage function in a new research project at the Medical Center.

"We want to determine what detrimental effects the virus has on monocytes and macrophages," says Dr. Landay. "These negative effects should occur before the virus goes on to infect the T-lymphocytes, when the disease becomes clinically obvious. The monocyte changes, which are very early on, might help us predict who among the people exposed to AIDS, but who don't have the disease, will go on to develop it someday."

"We also hope to get some understanding of the different stages of the disease," adds Harold A. Kessler, M.D., assistant professor of immunology/microbiology and a member of the research project's

team. "This way we could predict if someone is moving from one stage of infection to another. If we knew what moves an infected individual along the biological spectrum and what concurrent changes are taking place in his immune system, we could also predict how fast he'll move on to the advanced stage of the disease."

The two-year study is focusing on homosexual men from the Chicago area who are between the ages of 20 and 50. Fifty participants per year will have AIDS-related complex, a pre-AIDS condition, and 100 per year will be a control group of asymptomatic homosexual males.

"It's a two-phase study," notes Dr. Landay. "First, we want to look at the monocytes from the AIDS patients to evaluate whether the virus is in their monocytes and what changes have occurred in the function or surface features of these monocytes."

"Next, we want to take normal monocytes from healthy heterosexuals and intentionally infect them with the virus. This way, we'll be able to control the conditions and watch the monocyte functions. The eventual goal will be to successfully manipulate the cell so we can hold the virus in the monocyte phase. Or kill the virus. Or cause the cell to kill the virus. Or enhance the cell's immune function which might be deficient."

Much of the work on this study will be done in the Medical Center's new HIV Culture Facility. The first such hospital-based laboratory in the metropolitan Chicago area, the lab allows scientists to look directly at the virus in patients' cells.

"All the tests that we've used to date to look at infection with the virus really just let us look at the

footprints of the virus having been there," says Dr. Landay. "Culture studies let you look at the virus itself. Now we'll be in a position to prove that the actual presence of the virus, rather than just exposure to the virus, is associated with particular stages of the disease."

While studies such as this one can help scientists learn more about AIDS and predict which patients will become ill, other studies on this deadly disease have been concentrating on treating patients who already have AIDS.

"There are two main ways to fight AIDS," notes Dr. Kessler. "One is anti-viral therapy, finding a way to eliminate the virus. The other is immunological therapy, finding a way to sufficiently upgrade the immune system so that it can survive infection."

In recent months there's been a lot of publicity for one type of anti-viral therapy, a drug called AZT that's been found to prolong the lifespan of some AIDS patients. Research studies on the drug are currently underway, and Rush is participating in the testing of AZT with patients who've suffered from an infection called *Pneumocystis carinii* pneumonia, one of the most difficult infections to treat in AIDS patients and a frequent cause of their death. Nationwide studies on AZT will be ongoing to determine the safety, toxicity and efficacy of long-term use of AZT in AIDS patients.

"As a result of all the AIDS research, we've learned a tremendous amount about the immune system," notes Dr. Kessler. One day, that knowledge may translate into more effective therapy for AIDS patients, cancer victims, and people with other deadly diseases involving the immune system. J.P.

"Acute rejection occurs when you put any kind of organ from one member of a species into another member of the same species that is not an identical twin."

James W. Williams, M.D.

Transplant: Helping Enemies Become Friends

The immune response is not a thinking response. It's like a burglar alarm that goes off whenever someone crosses its path, unable to tell the difference between a friendly neighbor and a marauding thief. In the case of organ transplantation, the "invader" is necessary for life—and the immune system targets it for destruction.

"Acute rejection occurs when you put any kind of organ—skin, or a solid organ like the heart, kidney, or liver—from one member of a species into another member of

the same species that is not an identical twin," says James W. Williams, M.D., the Jack Fraser Smith professor of surgery, and director of the Section of Transplantation in the Department of General Surgery. Without immunosuppression, helper T-cells in the recipient's body recognize the foreign antigens on the donor organ, call killer T-cells to the attack, and destroy the organ within 10 days.

To prevent rejection, patients begin a lifelong low-dose course of immunosuppressant drugs, which interfere with the immune process. For example, the drug cyclosporine seems to prevent helper cells from producing a chemical messenger called interleukin II (IL-2), which would otherwise signal the killer cells to attack. Another method uses a newly developed

monoclonal antibody (OKT3), bound with complement, which seeks out and destroys T-cells.

If acute rejection does occur, physicians prescribe a high dose of immunosuppressants to stop the immune system in its tracks. For unknown reasons, the first acute rejection episode is also usually the last, and the patient can return to a lower, more tolerable level of immunosuppressants.

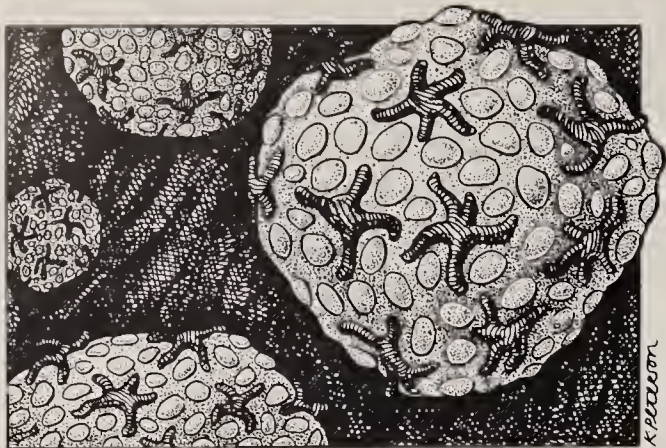
"This is the principle upon which all transplantation theory rests," Dr. Williams says. Immunosuppression impairs not only the body's ability to reject the organ, but also its ability to fight disease and infection. Indeed, the biggest risk to transplanted livers is not rejection, but infection. Therefore, physicians seek to keep immunosuppressant doses at their lowest possible level.

There's a second reason to keep the dose of immunosuppressants low, says Howard M. Gebel, Ph.D., associate professor of immunology/microbiology and director of the general immunology laboratory and of the histocompatibility laboratory. "Immunosuppressants, especially cyclosporine, have side effects that include renal and liver toxicity. It seems like a contradiction to transplant a kidney into a patient who is going to get a drug that has renal toxicity. Cyclosporine is not the panacea that people were predicting. It's still the best we have, but it's not enough," he says.

Dr. Gebel and Jeffrey Anderson, M.D., associate scientist and instructor of general surgery, are collaborating with Dr. Williams to develop a blood test to detect when



James W. Williams, M.D., examines a liver transplant patient.



Rush transplant immunologists are testing whether rejection can be prevented by eliminating Class II antigens (starfish shapes) from donor organs before they are transplanted.



Transplant immunologist Howard M. Gebel, Ph.D., is researching techniques to prevent the body from rejecting donor organs.

rejection is beginning. Current techniques are either invasive, such as a liver biopsy, or not highly reliable.

Using a device called a flow cytometer, researchers can count the number of cytotoxic T-cells (called CD8) which express an activation marker called CD25, indicating the cell has been readied for an attack. Healthy individuals and patients who aren't rejecting express very little CD25 on CD8 cells; even after their blood serum has been treated with a substance that encourages cells to express CD25, less than 20 percent of CD8 cells will. However, in transplant patients where rejection is beginning (as revealed by a liver biopsy), up to 60 percent of the CD8 cells express CD25.

"We've studied more than 200 samples and so far this simple, noninvasive blood test has been effective in determining if rejection has occurred," Dr. Gebel says.

"This has dramatic implications for transplant patients all over the world."

Acute rejection is not the only problem, however; transplant patients also suffer from chronic rejection. Acute rejection is caused by helper and killer T-cells. Chronic rejection is caused by B-cells, which produce antibodies against the transplanted organ.

"Chronic rejection occurs to some degree in almost all transplants that are not between identical twins," Dr. Williams says. "It's a slow process that may, over many years, cause the eventual loss of the organ. Furthermore, it's not treatable. Once the B-cells differentiate and begin producing antibodies against the donor organ, it's hard to turn them off. They become very set in their ways."

This problem is minimized through histocompatibility (HLA) matching. Genes on the sixth chro-

mosome encode HLA antigens. Class I antigens, which cause B-lymphocytes and plasma cells to produce antibody, are on all tissues except mature red blood cells. Class II antigens, which trigger cytotoxic lymphocytes to multiply, are principally found on cells involved with the immune response.

"Failure to match these HLA antigens is the major barrier to transplant success," Dr. Gebel says. "The odds of a perfect match for unrelated donors is very low. Siblings have a 25 percent chance to have identical HLA and a 50 percent chance of sharing half of their HLA antigens. Identical twins, of course, have identical chromosomes and therefore identical antigens."

Since everyone does not have an identical twin, perfect matches are rare. However, with histocompatibility testing, matches can be very close. In the laboratory, lymphocytes from the donor are mixed with serum from the intended recipient. If the recipient already has antibodies against the donor, the antibodies will bind to the cells, indicating that a transplant should not be performed.

"The one thing you never want to do is transplant a kidney or heart into a recipient who has circulating antibodies against the donor tissue. The antibodies attack, complement is activated, and the organ turns black and is destroyed, all in a matter of minutes. It's called a hyperacute rejection," Dr. Gebel says.

The problem is complicated by the fact that people who need transplants also tend to need fre-

quent blood transfusions. Each transfusion causes the body to produce antibodies against the antigens on the transfused blood.

"For many years, the dogma was to stay away from transfusions to decrease the odds that the patient would develop antibodies against potential donors," Dr. Gebel says. "Then a startling study was released about 10 years ago that showed the reverse was true: patients who received more transfusions tended to do better when they received kidney transplants, as long as they didn't have antibodies against the particular donor."

When the immune system is activated, suppressor T-cells are created along with the helper and killer cells so that the attack can be ended once the invader is destroyed. A similar reaction follows an antibody-mediated reaction, Dr. Williams explains; once the virus is destroyed, the B-cells continue to produce antibody for several weeks, then shut down. The circulating antibody gradually diminishes until only a few cells are left.

That suppression mechanism may explain why transfused patients do better, and why potential recipients who had antibodies against certain antigens at one point in time may not react several years later, Dr. Gebel says. "Perhaps the patient received a transfusion, made antibodies, didn't see those particular antigens again for years, and now the immune system fails to react. Or, perhaps some type of suppressor mechanism was activated so that the patient no longer makes antibodies against that antigen. This would be the ideal patient to receive the donor organ, since he or she is specifically not responding to the antigen."

Fooling the recipient's immune system by using these or other techniques is the goal of transplant immunologists like Dr. Gebel. Cyclosporine does this by impairing the helper T-cells' communication system; however, it must be taken daily for the rest of the patient's life, at a current cost of about \$7,000 a year.

Dr. Gebel and his colleagues are working to develop a technique in which immunosuppressants are given before the operation—and none after.

"In addition to pre-operative cyclosporine, we are using a reagent to eliminate all Class II antigens from the transplanted organ. If the transplanted organ doesn't express Class II antigens, the antibody won't hurt them," he explains. "The organ apparently doesn't create new donor antigens over time, since it is no longer in the donor."

In laboratory studies with rats, Dr. Gebel has successfully used this technique without post-operative immunosuppression to increase the survival of transplanted parathyroid glands from about 17 days (in a totally untreated animal) to well over one year. The lifespan of islet cells from the pancreas, which are more difficult to transplant, has been extended from 7 days to more than 50. "We're extending these studies now into heart and renal transplants," he says.

Reverse Rejection

The problem in bone marrow transplantation is exactly the opposite from any other type of transplant—instead of the recipient's body rejecting the transplant, the transplant rejects the recipient's body.

Bone marrow, located in cavities in the bone, produces blood cells, including the cells of the immune system. These cells are pro-

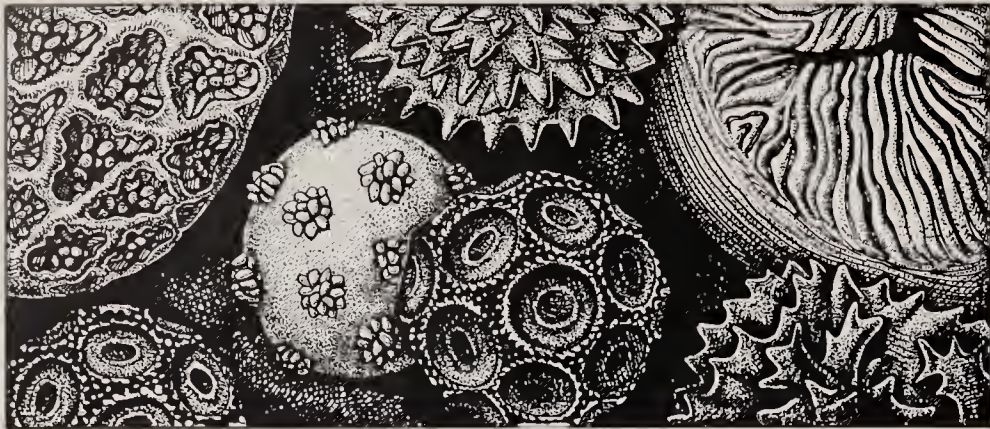
grammed to recognize the donor's antigens—and only those antigens—as friendly.

"The transplanted marrow recognizes its environment as foreign and sets up what we call graft versus host disease (GVH)," explains Herbert Kaizer, M.D., Ph.D., the Coleman/Fannie May Candies Foundation professor and director of The Thomas Hazen Thorne Bone Marrow Transplant Center. "It has two phases: acute, which is generally seen within the first three to four months after the transplant, and chronic, which can start as early as

six weeks or as long as a year after the transplant."

In acute GVH, the donor's lymphocytes identify the recipient as an "invader" and rally cytotoxic cells to the attack. For unknown reasons, the main targets are the liver, the intestines and the skin.

Chronic GVH is not as restricted; it will also attack exocrine glands—sweat, tear and salivary glands—the esophagus, and tissues within the lung. Patients with severe chronic GVH often have skin that is thick, scarred, and constricted at the joints, and that fails to provide a



Pollen grains enlarged to about 3,000 times the normal size



Herbert Kaizer, M.D., Ph.D., focuses on the problems of 'reverse rejection' with bone marrow transplants.

good barrier against infection.

Both types of GVH can be life threatening, and "the best way to treat them is to prevent them," Dr. Kaizer says.

One approach is to remove the mature lymphocytes from the donor marrow before the transplant. This is the most effective method of preventing GVH, Dr. Kaizer says, but a second problem quickly arises: the bone marrow is much more likely to be rejected by the recipient. In leukemia patients who receive bone marrow transplants, for instance, the rejection rate is about 1 percent. Using T-cell depleted marrow, the incidence of rejection is as high as 20 percent.

A second technique is to use immunosuppressive drugs for up to six months after the transplant. The mature lymphocytes gradually die off, and the new cells accept the recipient. However, the point of the transplant is to replace the recipient's malfunctioning immune system; suppressing the transplant continues to leave the patient vulnerable to infection.

And some GVH is a good thing, Dr. Kaizer adds. In addition to attacking healthy cells, transplanted lymphocytes also target leukemia cells or foreign invaders for destruction. Entirely suppressing GVH would give these cells a chance to proliferate.

The best approach would be to prevent GVH *and* target the leukemic cells for destruction. Dr. Kaizer and Herbert Chow, Ph.D., assistant professor of immunology/microbiology, are working on a monoclonal antibody that would immunize the patient against leukemic cells, readying the body's natural defenses against the invasion.

Vaccines operate by introducing a few weakened or killed invader cells into the patient, so that the antibody system can recognize it and organize its defenses against it. If the invader cannot be crippled, however, no vaccine can be made, since the vaccine would cause the disease before the host defenses could be readied. The quickly multiplying leukemic cells are a good example.

Drs. Kaizer and Chow are developing monoclonal antibodies that mimic the distinctive surface of a particular leukemia cell. The host's antibodies "recognize" the pattern and prepare the defense—without the introduction of the dangerous leukemia cells.

"We have now immunized rabbits and mice so that they produce antibody that seems to mimic the distinctive surface features of the leukemic cell. Now we can compare active immunotherapy (the monoclonals) versus other methods of treatment for leukemia," Dr. Kaizer says. "We have the feeling that this may be what we need to get rid of those last few malignant cells, making the bone marrow transplant treatment much more effective."

"Most allergies aren't life threatening—you are affected only in the areas where the antigen lands, such as in the nose and eyes for hay fever sufferers."

Larry Thomas, Ph.D.

Allergy: A Biological Mix-Up

An allergy is a mistake.

An allergic reaction occurs when the body mistakenly identifies harmless antigens as dangerous foreign invaders and triggers the immune system to attack, says Larry Thomas, Ph.D., assistant professor of immunology/microbiology.

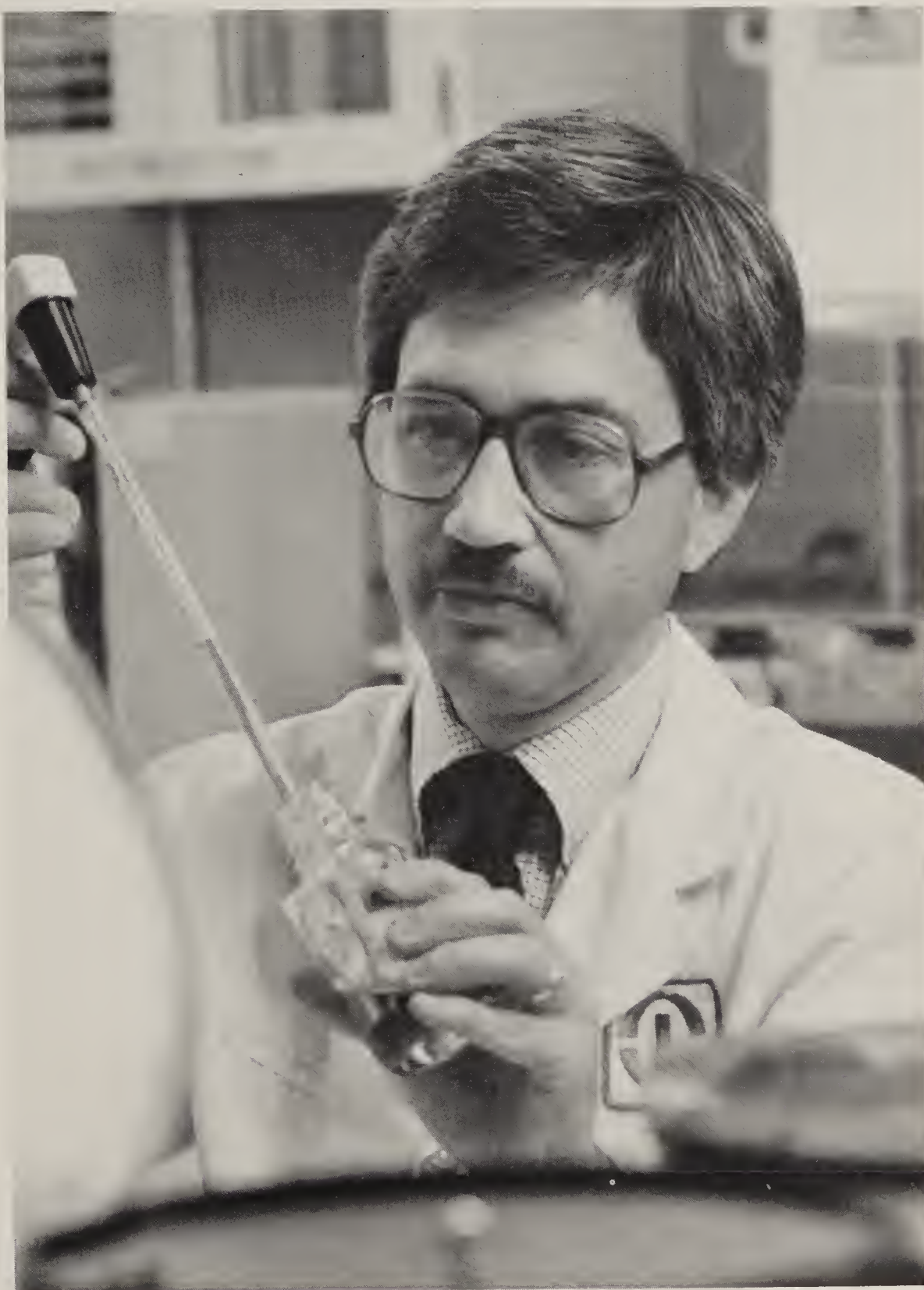
For example, hay fever sufferers produce an antibody called IgE, which circulates in the bloodstream until it settles on white cells called basophils and mast cells. A collection of these IgE antibodies sensitizes the cell to the foreign antigen, in this case ragweed pollen. When the pollen's antigen connects, or bridges, two or more of the IgE antibodies on the cell's surface, it triggers the cell to release two types of powerful chemicals—histamine and leukotrienes—which in turn cause the runny nose, itchy eyes, itchy skin and bronchospasms common in allergic reactions.

"Allergy has a genetic basis in that about 15 to 20 percent of the population has the capacity to make IgE antibodies against these naturally occurring antigens. Most people don't make IgE against those things," Dr. Thomas explains. "The current theory is that allergies are remnants of a bodily defense against parasitic infections, since all people have a very high IgE response to parasitic infections."

The allergic reaction can occur in two parts. The initial reaction—

also known as the immediate hypersensitivity reaction—occurs within 15 minutes of exposure to the foreign antigen and subsides in about 45 minutes (as long as the person is no longer exposed to the antigen).

However, the initial reaction may be followed by a late phase reaction, which occurs six to eight hours after the initial antigen exposure. In this case, while the basophils and mast cells are releasing their



An allergy is a case of 'mistaken identity,' explains Larry Thomas, Ph.D.

chemicals in the initial attack, they also send out chemical messengers calling other white cells, eosinophils, to the area. When eosinophils arrive several hours later, they deposit a substance called major basic protein, which triggers a second release of histamine and leukotrienes, causing a second allergic reaction.

Histamine and leukotrienes themselves are not "killers." Instead, they are part of the body's inflammatory response. They increase vascular permeability—"make the blood vessel walls more leaky"—so that the comparatively larger white cells can pass through and reach the invader.

"The IgE antibodies are vital under some circumstances, so we want to preserve them. We want to find out how to limit the allergic reaction through some type of drug intervention or immune therapy," Dr. Thomas says.

There are three methods. The first is to use a competing drug, such as an antihistamine. Histamine works by plugging into recognition sites on smooth muscles in the airway and in blood vessels, causing irritation and inflammation. Antihistamine works by occupying those sites before the histamine arrives, preventing the reaction. "The problem, of course, is that this doesn't work if the histamine release has already occurred," Dr. Thomas notes. Although no antileukotriene is on the market, several possible drugs are being investigated.

A second approach is to block the release of histamine and leukotrienes. Although there are prescription-only drugs which do this, they also, in effect, shut down this portion of the immune system.

The last method is immunotherapy shots. Allergy sufferers who are

periodically injected with small amounts of the offending antigen produce a second antibody, IgG. IgG binds with the foreign antigen before it reaches the IgE on the basophils and mast cells, thereby preventing the release of chemicals. Since IgG is present in the bloodstream in far greater concentrations than IgE, the allergic reaction is substantially diminished.

"This is very effective, especially for those who are allergic to insect stings," Dr. Thomas says. "Most allergies aren't life threatening—you are affected only in the areas where the antigen lands, such as in the nose and eyes for hay fever sufferers. But insect venom is injected directly into the bloodstream and causes a body-wide reaction, which in severe cases can cause death. Immunotherapy shots means that these people are now protected."

Dr. Thomas is continuing to study the late phase allergic reaction: "Our goal is to identify the parts of the interaction, find ways to control them and prevent chronic debilitating allergic disease." K.H.

Computers Advance Treatment and Learning at Medical Center

*By Jane Friedman
Gail Street*

Computers are now commonplace tools of hospital researchers and clinicians, as essential to diagnosis and treatment in many fields as an electrocardiogram or x-ray machine. At Rush-Presbyterian-St. Luke's Medical Center, immunologists, pathologists, biomedical engineers, educators and artists are advancing mainframe and computer technology into new realms, from animating videos of surgical procedures and chemical interactions to storing thousands of medical questions to designing metal hip joints.

Animated Procedure Design

Before computerized video animation, medical students and physicians viewed sequential photographs and line drawings of internal organs and systems to learn about surgical, anatomical and health-related procedures and diagnoses. Creating those drawings was time consuming and costly, according to Kurt Peterson, manager of the Medical Center's medical illustration and design department. As anatomically detailed as the drawings were, Peterson said, they still lacked the moving and probing



Kurt Peterson views his microcomputer as a design tool, like airbrushes and acetate.

parts necessary to mimic actual medical procedures.

Motion was eventually introduced to medical graphics through mainframe computers, but their prohibitive expense limited their availability for many institutions and medical departments on tight budgets, Peterson said.

Enter the personal computer, saving time, energy and money. "There was a time when everything was done on huge computers," Peterson related, "but now we're down to microcomputers with expansive memories that are much faster and less expensive than mainframes. We're now looking at micros as another tool, like airbrushes and acetate."

Video animation will provide "anatomical views and palpability that haven't been seen before," Peterson said. As an example, he cited the chemical action of a molecule as it crosses the rounded surface of a membrane. To represent that process, computer artists draw the molecule and the membrane surface on the computer screen, rotate the figures through space and, finally, bring them into contact, depicting the release of atoms and creation of a new molecule.

Animation will also play a role in medical education, according to Peterson. Students may soon be viewing computerized images of biopsies, representing a needle piercing a tissue, gathering a sample and retracting it. Peterson cautions that the animated segments will likely be brief, no more than 30-second spots incorporated into a videotape. But, he says, "animated video has the potential to be as revolutionary as *Fantastic Voyage* was or the early animation produced by the Walt Disney Studios."

From the world of uncharted computer potential, Peterson proffered another possibility—that computerized three dimensional pictures might allow scientists to visualize chemical interactions theorized but never seen. When particles placed into an electrical field are viewed through a photomicroscope, some, but not all of their activity might be observable, he said. Manipulating video images, he suggested, "might lend more credence to what scientists believe happens."

The medical illustrators in Peterson's department are creating their videos on a Cubicomp computer and an IBM-PC that exchange commands. With their computers, a digitizing tablet, a color and black and white monitor, the illustrators begin the animation process by drawing a one dimensional geometric figure such as a square, rendering or shading it, then expanding it to a 3-D cube on screen for viewing on all sides. Biological and human shapes, as well as other objects, can be added on the screen to build the computer model. Once a series of models is readied and sequenced, the computer, on instruction from the illustrator, will draw the required number of intermediary pictures. "The computer saves lots of time and energy, and," Peterson says knowingly, "relieves the artist's boredom."

Since February, Peterson's staff of two full-time medical illustrators has been experimenting and working hard to "keep up with the rampant pace of technology." When not busy with more standard graphics projects, they have been studying computer programs, learning the intricacies of microcomputer design and sequencing and drawing models of complex structures. Once they produce a sufficient

number of models, the demanding animation process will begin, requiring the illustrators' physiological and anatomical expertise as well as computer acumen.

With technology changing virtually everyday, video animators are uncertain, yet excited, about potential uses of their creations. Peterson is hopeful that the Medical Center's budget will be able to accommodate video animation costs and that researchers and educators will increasingly use this "unique approach to medical subject matter."

Color Coding Ultrasound Images

Medical illustrators are not the only people manipulating computer images at the Medical Center. The office of Jason C. Birnholz, M.D., professor, diagnostic radiology and nuclear medicine, inundated with terminals, screens, calculators and a four-foot tall color graphic camera, is testimony to his belief in the power and potential of computer technology.

As director of the Section of Ultrasound, Birnholz is using computers of various sizes, speed and memory capacity for traditional and innovative purposes—gathering patient information, converting ultrasound-obtained fetal dimensions into fetal weight, and adding subtle color gradations to black and white ultrasound images in order to discern diagnostically significant texture features. The latter, if as successful as Birnholz suspects, will be, he says, "a diagnostic breakthrough."

Ten years ago, there was a flurry of interest in colored ultrasound images but the endeavor had limited success, according to Dr. Birnholz. "The pictures were confusing, hard to organize, difficult to look at," he

"When information is buried in texture, color enhancement may be very helpful."

Jason Birnholz, M.D.

Jason Birnholz, M.D., is researching adding color to black and white ultrasound images to bring out hidden information.

says. "Directly color coded images could not be analyzed in detail; they were patchy and uneven and diagnostic information was often degraded."

In the intervening years, ultrasound images have become more highly detailed and smooth, in part because of computers. "All ultrasound images made here at the Medical Center are generated by computer," Dr. Birnholz explained. "That's a real big advance in equipment. We have five of the latest computed synography units, more than anyone else, and we were the first institution in the country to validate this new approach."

Until recently, ultrasound images were transferred directly from signal to screen without computer intervention. Today, computerized ultrasound machines sort data coming from the body and convert them to low-noise digital images that represent actual anatomy more closely. Adding color to that process, Dr. Birnholz believes, will increase the amount and quality of information revealed by ultrasound pictures.

Manipulating computer images is a "highly developed science that has been used exhaustively in enhancing satellite photos. Those studies use very large computers with sophisticated programming," Dr. Birnholz explained. "Even the smallest images are very complex and the information very large, so it's been difficult to do image processing on a small computer that can be purchased for personal or hospital use."

Dr. Birnholz has tried to over-



come the size problem by linking two computers, one very powerful and fast with a large image memory, and another, smaller, but capable of high-speed computations. While the big computer captures the television image, the small computer examines portions of the image for its texture. "We analyze very small portions, one step at a time, overlapping the fields so that eventually we have reviewed the whole image."

Color is the next stage. The tissue textures in each region, from smooth to rough and in between, are highlighted with a color. "I've been taking textured fields and analyzing their two-dimensional statistics," Dr. Birnholz said. "I then recode the numbers from the statistics as a color so that texture features are brought out. We start with black and white and shades of gray and end

up with color gradations overlaying the original. Some of this work was presented recently at an international meeting in Las Vegas."

Using color to bring out hidden information as opposed to simply coloring a black and white image, Dr. Birnholz said, is a new approach, one that is especially effective with liver ultrasound images. The texture features are "important diagnostically for distinguishing a cirrhotic liver from a healthy one," says Dr. Birnholz. Detecting atherosclerosis, industrial lung disease and other "hard to sort by eye" diseases of the thyroid, prostate, brain and breast are additional possible applications. "When information is buried in texture, color enhancement may be very helpful," Dr. Birnholz says.

"If our current plan seems to be helpful in clinical practice, the next

step will be to generate color images live as the study is obtained, as opposed to making a video tape and then running it through a computer some time later and analyzing it separately," he says. "This will involve close collaboration between our hospital and instrument manufacturers."

Dr. Birnholz's research and experimentation have made him a small computer enthusiast. "There is a lot you can do with small computers now. They are small and cheap in comparison with units when I was in school, but most are more powerful than their predecessors. There is no reason we shouldn't adapt them to medical imaging use." And, producing color ultrasound images, he says, "is a nice way to combine the two fields."

Expanding Flow Cytometry's Accessibility

Flow cytometry and the computer are like next door neighbors. They grew up together.

In the beginning, analyzing cells with a microscope, without flow cytometry and computers, was a slow and tedious process. It could take 20 minutes or more to gather information about less than a hundred cells.

Today, with recent technological advances, the equipment can analyze a thousand cells a second and collect four or more pieces of data about each cell. Also, the analysis is quantitative and objective, not subject to observer bias.

Cell analysis permits physicians to monitor patient progress; for example it can be used to check

transplant patients to determine if the body is rejecting the new organ, and to test AIDS patients to find out how their immune system is working. It also gives physicians an opportunity to look for cells which are indicative of lymph node cancer and leukemias.

Flow instruments enable investigators to look at the differences in cells through the use of a powerful laser optical system, which collects four signals from each cell simultaneously as it passes through the laser beam. A thin stream of fluid moves the cells rapidly in front of the laser, one at a time. Detectors pick up the fluorescent light signals. The computer handles all the data and does all the work of collecting the data.

Rush-Presbyterian-St. Luke's Medical Center is part of a nationwide network seeking to develop the best way to study exfoliated cells from bladders of patients who have had cancerous bladder tumors.

Network physicians will be using flow cytometry to diagnose the

presence of malignancy under circumstances which would not have allowed a diagnosis to be made using older methods.

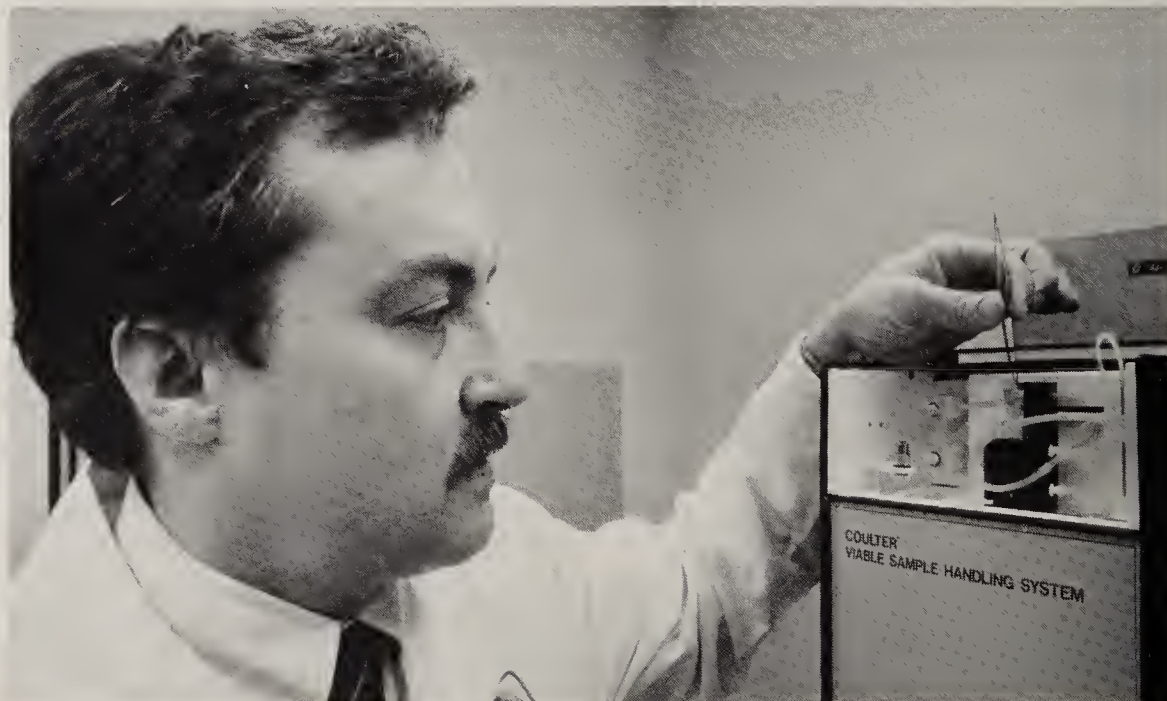
"Surgeons try to save the bladder wherever possible, so the entire bladder is not removed, only the tumor is resected," John S. Coon IV, M.D., Ph.D., associate professor, pathology, says. "But, after surgery, the patient risks developing recurring tumors."

Patients must be examined every six months after surgery, and interpreting examination results is often difficult.

"Many times tumor cells are hard to recognize, even for the most experienced cytologist," says Dr. Coon. "However, tumor cells characteristically have an abnormal DNA content. Measuring the amounts of DNA per cell is simple using flow instruments, but impossible to do by eye, even for the best pathologist."

In normal cells the amount of DNA is very closely regulated. Normal cells all have the same amount of DNA within about one percent.

John S. Coon IV, M.D., Ph.D., inserts cancer cells into the flow cytometer to analyze their DNA.



"Measuring the amounts of DNA per cell is simple using flow instruments, but impossible to do by eye, even for the best pathologist."

John S. Coon, IV, M.D., Ph.D.

But in tumorous cells, the amount of DNA is often abnormal. Pathologists have found they can sometimes predict how far the tumor is likely to have spread by the DNA content.

By combining the data extracted by the flow cytometer and compiled by the computer, a quantitative analysis of the tumor cells can be made. This helps the physician determine the patient's prognosis and treatment regimen.

"One additional advantage we will have here at Rush is the direct off-line data analysis, using an IBM XT computer system," says Alan Landay, Ph.D., assistant professor, immunology and microbiology and director of the Flow Cytometry Laboratory. "If we can do data analysis in our own offices, we can dedicate the flow lab instrument to do experiments, thus increase the volume of patient diagnoses."

In order to design the computer programs needed to make information more accessible, Drs. Coon and Landay called in a computer specialist, Dr. Howard Shapiro, of the Harvard Center for Blood Research.

What the trio came up with is a "black box" or interface which converts the signals from the flow cytometry computer into information an IBM personal computer can understand and use.

With the computer installed and the interface in hand, they are now working on software for processing the data.

"We want to develop a model for general application that can be shared among all hospitals. Anyone will be able to use a simple version of our system and save money," says Dr. Landay.

And within the next six months, Rush's own system will be up and running.

Computer Assisted Prosthetic Design

Artificial hips came along in the late 60s, knees in the early 70s, elbows by the mid 70s and wrists by the late 70s. And even though joint replacement remains a "modern day miracle" for arthritics suffering from debilitating pain in the 80s, doctors continue to search for a "better way."

In the past, hip implants or prosthesis were placed in a bed of cement, so sizing was not particularly important. Implants came from a stock of specific sizes and shapes, and gave the patient a sort of "off the rack fit."

But with technological advances in prosthesis design, it's becoming necessary to fit the implant like a new shoe to a foot. Custom-made implants must be ordered. Soon orthopedic surgeons at Rush will use their computer to design replacements to fit individual needs.

Jorge O. Galante, M.D., the William A. Hark, M.D.-Susanne G. Swift professor and chairman, orthopedic surgery, expects to use the computer to design metal hip joints when diseased or broken natural hips have to be removed or replaced. This "custom fitting" is especially crucial in revision surgery—operations correcting problems caused by previous implant surgery.

Computer-Assisted Design (CAD) has been used in industry ever since researchers realized that a computer can not only manipulate numbers and words on its screen, but also lines which represent images. These lines are capable of providing not only two-dimensional but also three-dimensional images of real objects. The images are in full color and can be

manipulated so as to appear to turn or rotate in space. In fact, CAD is used for special effects in the filming of space adventure movies.

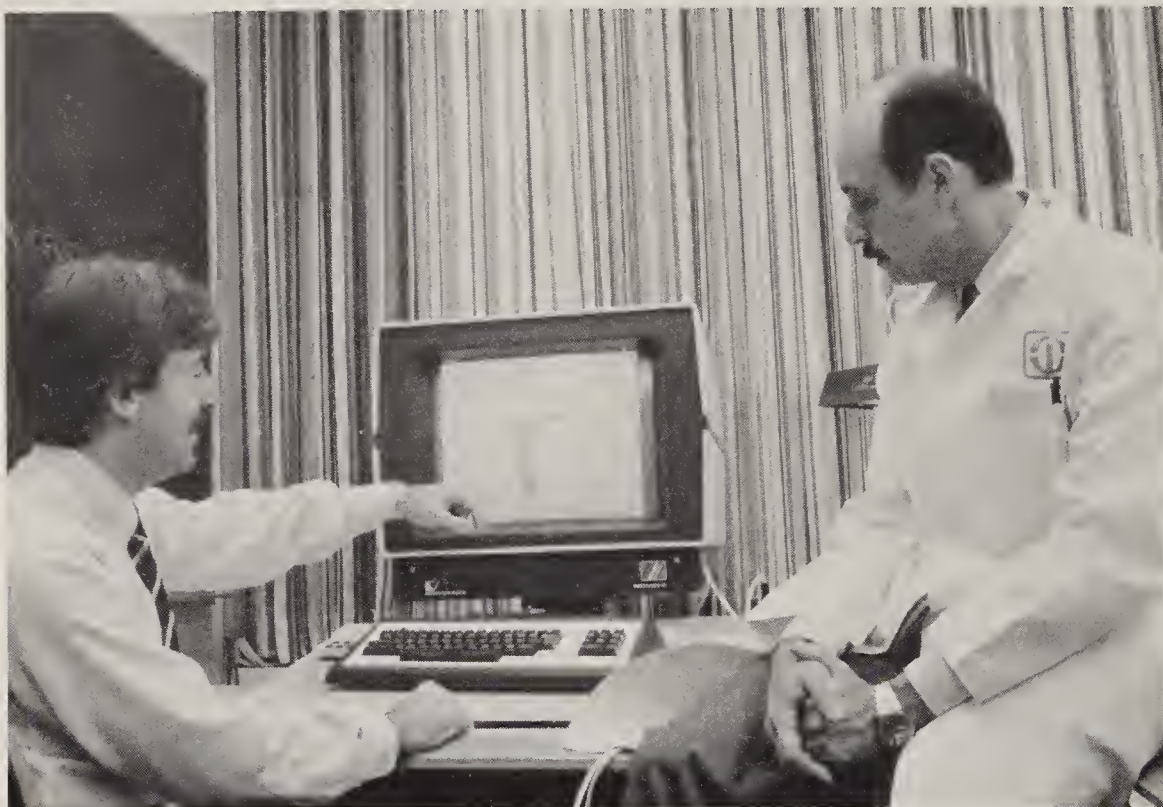
Right now CAD is being used at Rush-Presbyterian-St. Luke's to assist surgeons with hip surgery. Thomas P. Andriacchi, Ph.D., professor of orthopedic surgery and director of the Medical Center's John L. and Beatrice Keeshin Human Motion Research Lab, and his staff of researchers use the digitalized information from CT scans, information the computer can understand and translate, to form three-dimensional images of living structures. In the case of surgery to fix a malformed hip bone, for example, CT scans would be made of the femur or thigh bone. That data is fed into the design computer and manipulated, so that images of the bone are isolated from muscle and other tissue. Pictures of the bare bone are then displayed, rotated and studied on the screen by the surgeons who will attempt to fix it.

The computer makes it possible for physicians to visually remove sections of the bone and place them in new positions on the computer screen, until the computer indicates which combination of removing and replacing would lead to the most successful surgical outcome.

Other anticipated uses for computer-assisted design include:

- Achieving more perfect matches than at present between banked bones and the spaces they are to fill in healthy bone after a cancerous segment has been removed.
- Compiling the precise information necessary in the reconstruction of faces marred by malformation, accidental injury, or cancer surgery.

"Furthermore," says Dr. Andriac-



Thomas P. Andriacchi, Ph.D., and Jorge Galante, M.D., study computer image of patient's hip joint.

chi, "we plan to combine resources of this computer with our computer in the Gait Laboratory to define better which alterations in the bone affect forces and motions applied in walking, running and climbing."

Identifying Gait Problems

The Gait Analysis Laboratory in the John L. and Beatrice Keeshin Human Motion Research Laboratory is one of the nation's few sophisticated resources for analyzing the walking and climbing motions of the human body. It is an integral part of the total orthopedics program, and has been the focus of engineering research at Rush since the mid 70s.

Here researchers study loads, forces and stresses on implants which have malfunctioned, to determine whether the cause is structural failure or stress related.

"If you are going to do reconstructive surgery on joints you have to know how the procedure and

the implant affect joints and movement in patients," according to Thomas P. Andriacchi, Ph.D. "Ultimately, how the patient functions with the prosthesis will tell you how good the procedure was. But the subjective response by the patient is not enough. The gait lab allows us to quantitate the results in scientific studies."

Computers evaluate the recovery of patients with joint disease, who have prosthesis such as total knee replacements.

Dr. Andriacchi has analyzed knees in more than 100 patients and his computer graphics show how close each design comes to the workings of a normal knee. In fact, the computer chooses patients for some knee surgeries, such as the procedure to correct a form of bowlegs associated with arthritis. And, every patient it has selected as a potentially successful candidate for the surgery has actually had a successful outcome.

In the past, data from x-ray films of the patient's legs were made while the patient stood still. The data, however, did not take into consideration what happened during the walking movement. To assess this better, Dr. Andriacchi put 21 bow-kneed arthritis patients, scheduled for surgery, through the gait lab. Light emitting diodes (LEDs) were hooked to each patient's pelvis, hip, knee, ankle and heel and to the base of the foot. Cameras recorded the movement of the LEDs and relayed images of the patient's gait into a video display terminal. From that image, computers calculated the various angles of the flexed knee joint and the amount of mechanical force acting on the joint. By combining this data with the patient's own comments, Dr. Andriacchi is able to identify problems. Patients in the study were also tested a year after the knee surgery and again three years later.

What researchers discovered was a shift of weight toward the center of the body during walking that was predictive of success. In terms of motion, the shift is called the "adduction moment." And the research team found that the lower the adduction moment, the better results after surgery.

Simply stated, the low adduction patients exert lower compressive forces on the inner parts of the knee. This appears to be a way for an arthritic patient to compensate for a knee deformity. The result is a gait of shorter-than-normal stride.

By contrast, the more normal stride of the high adduction patients

INSIGHTS

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INTO CLINICAL AND SCIENTIFIC PROGRESS IN MEDICINE

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Enhancing Nerve Regeneration

Nerves of the peripheral nervous system have the capacity to regenerate after an injury. What remains problematic is the time that it takes these injured nerves to repair themselves (they grow only 1 to 4 millimeters a day) and the limited ability of injured peripheral nerves to reconnect themselves with their appropriate peripheral targets.

By studying different types of nerve injury and testing various surgical techniques of repair, James Kerns, Ph.D., assistant professor, anatomy, Rush-Presbyterian-St. Luke's Medical Center, and his colleagues hope to discover effective methods to stimulate and improve peripheral nerve regeneration.

Nerves of the peripheral nervous system connect the central nervous system (brain and spinal cord) to other body organs. Peripheral nerves are made up of both sensory and motor fibers called axons, which arise from neuron cell bodies. Schwann cells form a supportive tube through which the axons pass.

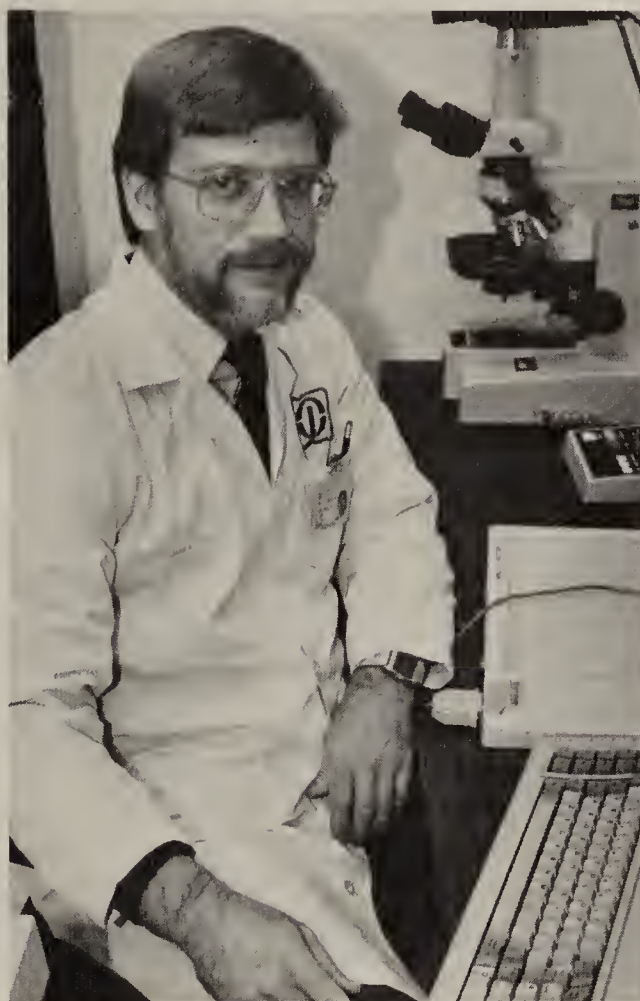
When a nerve is injured, Schwann cells play an important role, preparing the degenerated (distal) stump to receive the axonal sprouts coming from the healthy (proximal) segment. The sprouts which successfully cross the lesion gap will go down the tube formed by the Schwann cells and may innervate the appropriate target muscle or skin. Those that do not successfully traverse the gap proliferate and form a knot of fibers called a neuroma, which inhibits functional recovery and may cause severe pain.

"A successful reinnervation depends on several factors," Dr. Kerns says. "A primary focus of our research is on repairs which might enhance recovery."

Using laboratory rats as animal models, Rush researchers studied two types of sciatic nerve injury—crushed and transection.

According to Dr. Kerns, "the gap in the crushed nerve is very small and the axons from the proximal stump can easily grow into the distal stump, successfully innervating the target without any assistance. Disruption in the continuity of the nerve, as seen by light and electron microscopy, is minimal."

"In a transected nerve, however, most of



James Kerns, Ph.D.

the regrowing axons have problems crossing the gap, which is much wider and more scarred. They become blocked and form a neuroma."

Dr. Kerns and his colleagues tested two types of repair for the transected nerve: conventional microsurgery using two 10-0 epineurial sutures, and a newer surgical technique (developed by Luis deMedinaceli, M.D., St. Elizabeth's Hospital, Washington, D.C.) designed to reduce the tension and distance between the cut ends of the nerve axons.

To evaluate the effectiveness of these two repair procedures, Dr. Kerns and his colleagues studied the actual functional recovery of the rats and monitored the anatomical regeneration of the nerve.

The Sciatic Functional Index (SFI), developed by Dr. deMedinaceli, was used to evaluate the sensory and motor functional return of the injured sciatic nerve. Researchers analyzed the rats' walking tracks and gait to evaluate the extent of functional

deficit as the animals recovered. Results indicated that rats with crushed sciatic nerves returned to normal walking behavior after about three weeks. The group with transection injuries and conventional repair had a poor recovery; the deMedinaceli-technique group were only slightly improved.

To isolate motor from sensory recovery results, Rush researchers developed a new procedure which measured the twitch tension of muscle fibers. They found that the motor function of the crushed lesion group again recovered within the first month, but the transection with conventional repair group continued to have a poor recovery. However, the recovery in the transection group with the deMedinaceli repair more closely approximated that of the crushed injury group.

"It appears that motor nerve regeneration and function is enhanced to a greater extent than sensory recovery using the deMedinaceli technique," Dr. Kerns says. "This is in keeping with the current thought that muscle strength will recover much more quickly than sensory feeling such as touch or pain."

Researchers used nerve morphometry and a retrograde tracer to study the structural regeneration of the nerve fiber. The morphometric analysis of the nerve included counting the fibers, measuring fiber diameters to obtain nerve fiber density and tracking the maturation of the myelin sheath, an axonal covering produced by the Schwann cells to enhance the conduction of nerve impulses.

"The transection with conventional repair group showed severe degeneration at 32 days. At the same time, both the crushed nerve group without any intervention and the deMedinaceli reconnection group showed improvement with the presence of axons with thicker myelin sheaths," Dr. Kerns says. By using a retrograde tracer (horseradish peroxidase) Dr. Kerns and his colleagues were able to prove quantitatively that there was a reduced number of regenerated neurons in the transection groups.

"Overall, we found that the axonal sprouts had increased in number but were reduced in size and that there was a 30 percent reduction in the number of neurons," he says. "This correlated with the decreased

function that we found in the behavioral locomotion and the twitch tension." These functional and structural methods utilize computerized analysis and are being used to accurately assess many different peripheral neuropathies, such as the chronic effects of local anesthetics on nerve, a clinical application of recent interest."

In another approach to further enhance nerve regeneration, the researchers applied a DC electrical field to the transected sciatic nerve through an electrical implant. "Seven days after injury and insertion of the implant the regenerating axons which had been exposed to the continuous electrical current had grown 68 percent further into the distal segment than those axons which had not received the treatment," Dr. Kerns says.

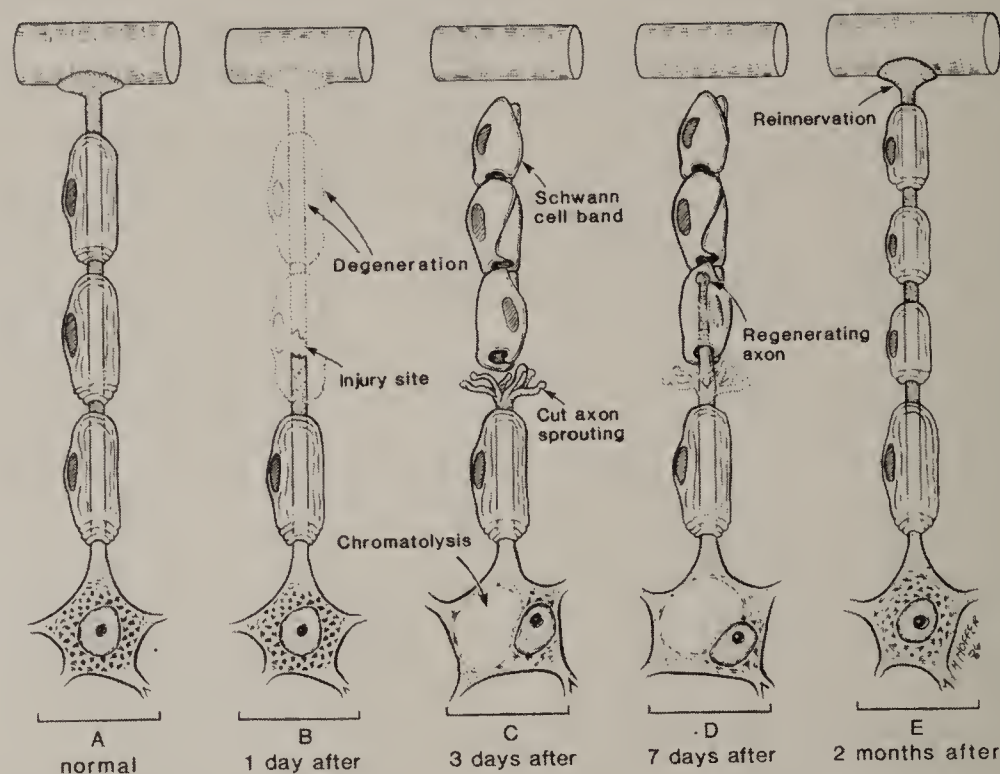
"We've only begun to figure out how we can promote nerve regeneration," he says. "We hope that the principles that are learned in the peripheral nervous system will aid in the understanding of the even more difficult questions involved in the regeneration of the brain and spinal cord."

Mary-Ann Redeker

Collaborating with Dr. Kerns in this research are: Harry Weinrib, M.D., Ph.D., instructor, plastic and reconstructive surgery; John Freeman, M.D., Ph.D., Vanderbilt University; Luis deMedinaceli, M.D., St. Elizabeth's Hospital, Washington, D.C.; and Jeffery S. Kroin, Ph.D., associate professor, neurosurgery. Funding for this research came from the National Institute of Neurological and Communicative Disorders and Stroke of the National Institutes of Health.

Examining the Link Between Alcohol and Good Cholesterol

Levels of high density lipoprotein cholesterol (HDL), the "good cholesterol" that has been linked to a lower risk of coronary artery disease, rise after alcohol is consumed. When drinking is discontinued, the levels drop off. Exactly what causes this increase and decline is the focus of research headed by Seymour M. Sabesin, M.D., the Josephine Dyrenforth professor of gastroenterology and director, digestive diseases, at Rush-Presbyterian-St. Luke's Medical Center.



When a normal motor neuron (A) is injured (B), the distal segment degenerates and the proximal axon grows several sprouts (C), some of which grow into the reformed distal Schwann cells (D) and reinnervate the muscle (E).

Most of the body's cholesterol, a fat-like steroid alcohol present in all body cells, is synthesized by the liver; only a small portion is contributed by diet. Dr. Sabesin and his colleagues are searching for the biochemical mechanism by which HDL levels increase with chronic alcohol intake.

"If we can determine the mechanism," Dr. Sabesin explains, "we may someday be able to mimic the effect of alcohol, and raise HDL levels to reduce risks for development of atherosclerosis."

Dr. Sabesin and his colleagues are conducting three separate studies with male social drinkers and alcoholics for clues to the rate and path of HDL synthesis.

The first study looks at changes in lipoprotein levels and composition accompanying alcohol ingestion in moderate drinkers.

Currently, two mechanisms seem most likely for the elevation of HDL by alcohol, Dr. Sabesin says.

"It may be that alcohol simply induces the liver to manufacture more HDL by increasing synthesis or activity of the

enzymes responsible for this production," he explains. "The liver's ability to synthesize HDL is proportional to the liver's clearance of the drug, antipyrine. Thus, the rate at which this drug is eliminated into the blood after intravenous injection (IV), is a measure of the liver's HDL production."

Another possible explanation is that alcohol causes an increase in the clearance of triglyceride-rich lipoproteins into the blood. "We know that the clearance of these fat particles produces HDL components," Dr. Sabesin adds. "This clearance pathway involves two enzymes—lipoprotein lipase and liver lipase."

Dr. Sabesin measured blood levels of lipoprotein lipase and liver lipase following an IV injection of the anti-coagulant heparin, which displaces lipase from cell surfaces into blood so that the enzyme levels may be measured. He then correlated the changes with changes in post-heparin lipase activity.

During the testing, ten healthy male social drinkers abstained from liquor for two weeks, drank 60 grams of alcohol per day for the following three weeks, and

abstained again for two more weeks. At the end of each period, participants received heparin and antipyrine. HDL was measured every week.

Analyzing HDL levels during all three periods, Dr. Sabesin confirmed that HDL rose significantly during periods of drinking alcohol. The drug data, which are still being studied, could clarify the mechanism of HDL production because, as Dr. Sabesin says, "the clearance of these drugs is a measure of the activity of enzymes that synthesize HDL."

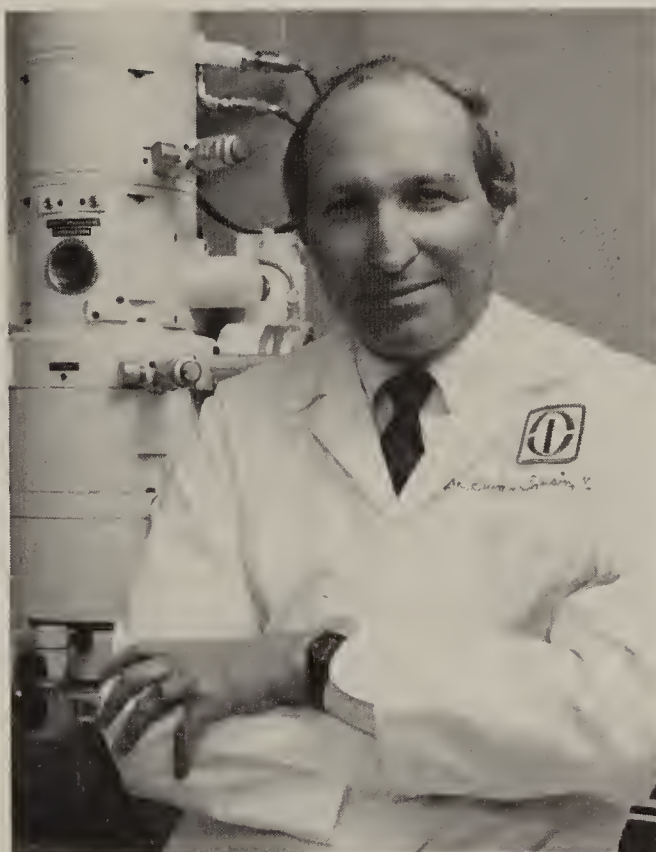
A second study will examine HDL production in chronic alcoholics who have elevated HDL cholesterol with little evidence of liver disease. Several parameters will be measured including lipoprotein levels and composition, post-heparin lipase activity, and the rate at which orally administered triglyceride (TG) is cleared in the blood.

During the two-week testing period, ten alcoholic subjects, who voluntarily admit themselves to a detoxification center, will drink a high-fat egg and cream "milkshake" and then have their blood drawn periodically to assess triglyceride clearance. Post-heparin lipases also will be measured.

"We're assaying the activity of the two triglyceride lipases present to determine whether alcoholics' post-heparin lipase levels are abnormally high," Dr. Sabesin explains. "If it is, the clearance of oral fat should follow the same pattern as the lipases. It should be faster when subjects have just gone off alcohol. If the levels return to normal when they abstain from alcohol, these findings would back up the first study's results."

The third study will measure the effect of alcohol on the clearance of triglyceride-rich lipoproteins in ten healthy social drinkers who imbibe less than six ounces of 100-proof alcohol daily. Because the fat will be introduced directly into the intestine at a constant rate, Dr. Sabesin will be able to estimate the clearance of the triglyceride-rich particles as they are absorbed by the intestine and secreted into the blood. After the participants drink alcohol, the change in TG clearance will be measured and should shed light on the acute effect alcohol has on TG clearance.

"The results may support the theory that HDL levels rise with alcohol due to increased synthesis and secretion of triglycerides by



Seymour M. Sabesin, M.D.

the intestine in response to ingested fat and subsequent rise in TG clearance," Dr. Sabesin says. Hence, more HDL components are generated.

Results of these studies may break new ground. "No one before has looked at the effect of alcohol on the HDL subspecies along with HDL synthesis assessed by antipyrine clearance," Dr. Sabesin says. "We hope this will give us new insights."

Jane Friedman

Collaborating with Dr. Sabesin in this research are: Stuart W. Weidman, Ph.D., professor, medicine; William Evans, Pharm. D., professor and chairman, clinical pharmacy, University of Tennessee Center for the Health Sciences, and director, pharmaceutical sciences, St. Jude's Hospital; Vicki Rouse, M.S., lab supervisor, Digestive Diseases Research Laboratory; and Mary Ann Linderman, lab technician.

Improving IVF Techniques

The in vitro fertilization and clinical pregnancy rate for human beings is at best 24 percent. To try to improve that rate, physicians and researchers rely on animal models to test various techniques.

"We see problems in the IVF lab that we can't solve using human embryos in research. It would be both unethical and illegal," says Richard Rawlins, Ph.D., assistant professor, obstetrics and gynecology, and co-director of the In Vitro Fertilization Laboratory at Rush-Presbyterian-St. Luke's Medical Center.

"But we can use animal models to develop optimal culture conditions for incubating the egg, and to improve the timing of the transfer to increase the implantation rate."

Dr. Rawlins is using rhesus monkeys in IVF research. He is also experimenting with separating embryo cells and exploring techniques for detecting genetic abnormalities.

The rhesus monkey is a good study model because it has a 28-day menstrual cycle and is physiologically similar to humans, Dr. Rawlins explains.

The IVF process for the monkey is also similar to that used for humans. After the monkey receives shots of follicle stimulating hormone and human chorionic gonadotropin (donated by the Serono Corporation) to stimulate egg development, the eggs are retrieved through laparoscopy: a thin tube containing fiber optics is inserted into the monkey's abdomen and the eggs withdrawn using a needle.

"Just as you can continually do laparoscopies on humans, you can do them on animals without causing any damage," Dr. Rawlins stresses. "This research is non-destructive; there's no real pain or distress for any animal involved in the program."

The eggs are put in a culture dish to further mature, and the sperm is added a few hours later. Researchers check the eggs in about 12 to 16 hours to see if they are fertilized. At 24 hours, the embryo divides for the first time, and repeats the process every 12 hours.

Between 48 and 72 hours after fertilization, researchers can attempt another technique: embryo-splitting. Using a micromanipulator (a tiny glass needle probe powered by a hydraulic system similar to a videogame joystick), researchers can separate an embryo's cells. The cell groups will then develop into identical twins, triplets or quadruplets, each with the same chromosomal makeup.

"At this stage, the embryonic cells, unlike those in any adult, human or animal, are

not specialized in any way. If one cell dies, the others compensate for it, and the embryo develops normally," Dr. Rawlins explains. "Therefore, you can separate those cells and have several embryos develop."

Once the separated cells have divided sufficiently, they can be implanted in the mother's uterus—or in the uterus of a biologically similar surrogate mother. A single fertilized egg could conceivably become four rhesus monkeys.

Or, one of those cells could be karyotyped—broken down and chromosomally analyzed—to check for major genetic abnormalities. For example, it's possible for an egg to be fertilized by more than one sperm. The cell would grow and divide for some time before it would be spontaneously aborted. Karyotyping would allow these abnormal embryos to be identified before they were implanted in the mother.

"From these studies we hope to develop ways of identifying faulty eggs before making the transfer, eliminating false hopes of a successful pregnancy for our IVF patients," he says.

Embryo-splitting isn't new. In the late 1880s, German anatomists first tried splitting apart a sea urchin embryo. They succeeded, and the work progressed through amphibians to mammals. In 1979, scientists at Cambridge University in England were the first to split sheep and cattle embryos into two or four groups, then transfer them to surrogate mothers.

However, induced twinning has not been successfully done in primates, in part because the implantation of the egg in the uterus wall is physiologically different and occurs more quickly. "In cattle, the implantation



Richard Rawlins, Ph.D.

rate is 80 to 85 percent, probably because embryos normally go through a free-floating phase for four to five days," Dr. Rawlins explains. "The timing of embryo transfer is less crucial than in primates and humans."

Of course, embryo splitting would not be done on humans, but the ability to twin primates could benefit both humans and animals, Dr. Rawlins says.

"By twinning primates, we can get animals that are very valuable for genetic control in experimental research. Secondly, for endangered species or species that are biologically unique, we can rapidly expand

the pool of animals available. A monkey mother might normally give birth 10 times in 13 years. By introducing this type of high-tech biology and using surrogate mothers, we can triple the number of animal offspring."

Kris Hansen

Collaborating with Dr. Rawlins on this project are: Zvi Binor, M.D., assistant professor, obstetrics and gynecology; W. Paul Dmowski, M.D., Ph.D., professor, obstetrics and gynecology; and George D. Wilbanks, M.D., the John M. Simpson professor and chairman, obstetrics and gynecology.

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"If you are going to do reconstructive surgery on joints you have to know how the procedure and the implant affect joints and movement in patients."

Thomas P. Andriacchi, Ph.D.

does not compensate to relieve forces on the knee. Dr. Andriacchi believes this non-compensating gait is an important factor in the failure of surgery for the high adduction patients.

Over the past five years, bio-mechanical researchers have used the gait lab to evaluate different artificial knee prosthesis designs, in a study funded by the National Institutes of Health.

Over 100 patients received various types of implants and were tested in the human motion lab, first walking on flat surfaces and then climbing stairs. From these tests, Dr. Andriacchi was able to identify a knee prosthesis design that allowed for the best active movement as well as those that hindered movement the most and why.

In addition to evaluating prosthetic design, laboratory researchers also do stress analysis tests of the materials that make up orthopedic implants.

Dr. Andriacchi is conducting studies using the three-dimensional optical digitizer. This is an instrument developed in Sweden. Rush is the first and only place in the United States to use it. The digitizer provides mechanical information on how lower extremities move. It tracks the position of small light emitting diodes placed on each subject's shank, thigh and foot.

The information is fed directly into a computer which translates it into the computer word. In the past, it was necessary to take photographs of the limbs and then measure the photographs. Now these jobs are completely automated.

Computer Based Education

At Rush University, students and faculty are also benefitting from innovative software, chiefly through efforts of the Office of Computer Based Education (CBE), which has written an electronic logbook and integrated it with an item banking/test delivery evaluation system for clinical training. The system, now being used by the Department of Medicine, and first tested at the University of Illinois, eliminates enormous amounts of administrative paperwork and allows medical students to test their knowledge on a variety of diseases they have encountered during their 12-week internal medicine clerkship.

Developed by the University of Illinois and Rush University as a test item storage bank for the Midwest Association for Education Resource Sharing in Clinical Medical Technology, the system allowed professional staff easy access to a pool of medical technology questions. The expanded version, now in use at Rush, classifies items in a hierarchical format, subdividing major topics into up to eight subsets

such as diagnostic methods, clinical syndromes, specific disorders and specific diseases. Questions in any of these areas, as many as 99 in some, can be retrieved by students for self-assessment in three different formats: tailored to the particular diagnoses the student has experienced during his/her clinical visits, selected from any or all diagnostic areas or chosen randomly by the computer.

"Our goal is to help the instructor deliver better quality instruction and to provide students with every available resource," said Victoria Moore, director, Computer Based Education. "The item bank is an educational enhancement."

A second aspect of the CBE-written software is the electronic logbook, an administrative time-saver used last year by medicine to record students' activities at clinical sites during their clerkship. "The program tabulates, generates reports, totals the number of procedures at each site, lists patients' floor locations and relieves administrators of lots of managerial work," Moore said.



Victoria Moore displays software available in computer based education.

"I used to have a set of 40 books and I'd have to read each one. This way, I get one printout balancing the whole year, telling me what individuals and groups of students have done..."

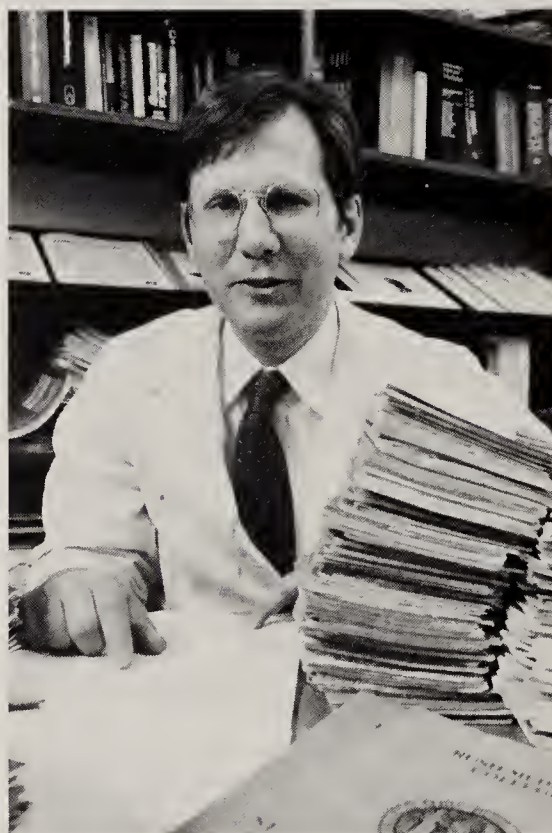
Robert Rosen, M.D.

Computer printout now gives Robert Rosen, M.D., information he formerly culled from stack of student bluebooks.

Robert Rosen, M.D., assistant chairman of the Department of Internal Medicine and director, educational affairs, concurs with Moore's assessment. All students in the internal medicine clerkship used the logbook during the past academic year. Rather than pouring over student blue books detailing students' experiences and procedures performed (e.g., abdominal paracentesis, defibrillation, urethral catheterization, peritoneal dialysis), Rosen was able to call up the information on the computer, already tabulated. "The electronic logbook makes it easier to look at which patients students are seeing here and at alternative locations," Rosen said. "I used to have a set of 40 books and I'd have to read each one. This way, I get one printout balancing the whole year, telling me both what individuals and groups of students have done so I can be sure no bad trends are occurring."

All internal medicine students are again using the logbook this academic year. A group of medical students is, for the first time, experimenting with the item banking feature. "We will evaluate whether the addition of this resource has an impact on students' scores on the miniboard at the end of the internal medicine rotation," Moore said.

The University's access to the item bank comes through the University of Illinois' PLATO, a computerized educational teaching system purchased by the Medical Center and other public and private teaching institutions. Students use



IBM computer terminals, located on the three major student floors in Presbyterian-St. Luke's Hospital and in physician lounges, to enter the major and minor diagnoses they have seen, record their notes, all procedures performed, assisted with or observed and any additional comments. At any time during their clerkship, the students can generate a computer menu of broad diagnoses as well as specific disease entities.

When the system is fully operational, a typical request for an exam about renal/electrolyte diseases could elicit as many as 99 questions on diagnostic methods such as urinalysis and blood studies, clinical syndromes such as hematuria and dysuria, disorders of electrolyte and acid-base balance such as hyponatremia and hyperkalemia, and specific renal diseases including interstitial nephritis and toxic nephropathy.

"Students traditionally got a very general exam but, because they were at six different sites, they never all saw the same patients. Now they can be tested on the specific things they've seen," Moore explained.

The test questions come from three sources: physicians, old tests no longer in use and board examinations. Because the program generates a statistical analysis of each question, programmers and professors are able to determine the value of each one and eliminate those deemed poor.

Although student access to the electronic logbook and test items is through personal size computers and IBM software that emulates PLATO, Moore believes the program in its present form will likely remain on a mainframe computer because of its size and complexity. "This is a massive program because of the number of questions and options associated with it. One program tallies, another prints reports. There are so many components of the program that it belongs on a mainframe," she said. The logbook portion could, however, be adapted for personal computers, Moore speculated, if students had their own data disks or access to a mainframe like PLATO.

Moore foresees a time when other Rush University departments will use the logbook to track their students and store old examinations and when residents will record patient notes daily. If the item banking system, now operating only at Rush, proves educationally advantageous, it will undoubtedly become a component of other medical school curricula. When that happens, the system will prove to be, as Moore says, "truly unique and revolutionary."

Medical Center Staffers Give Aid Around the World

In recent months medical and nursing staff members of the Medical Center have provided care and comfort to the sick and injured in many parts of the world. The following articles detail some of their experiences:

In Afghanistan

"I'd been interested in doing medical work in an underdeveloped country for some time, just for the experience of working in a foreign culture and helping people," said Judd Jensen, M.D., assistant professor and adjunct attending physician, neurology, Rush-Presbyterian-St. Luke's Medical Center.

That desire led him to volunteer for a relief team to Afghanistan, which has been torn by civil war since Soviet troops entered the country in 1979. The Soviets

expelled the Red Cross and all other medical relief organizations, so French, German, Belgian and American medical teams have been smuggled in to treat the sick and injured. Dr. Jensen's two-month trip was organized by International Medical Corps and funded by American Aid for Afghans, both private groups.

"Although we heard the Soviets were committed to killing foreigners on sight, our team was destined for an area controlled by the freedom fighters. We also knew we'd be traveling with bodyguards, so we thought we'd be relatively safe as long as we stayed out of the cities," Dr. Jensen reasoned.

After an extensive briefing in the United States, the team arrived in Peshawar, Pakistan, last summer on August 11, 1985. It included Dr. Jensen; John Moughan, R.N., from Winter Park Memorial Hospital,



Judd Jensen, M.D., (right) and John Moughan, R.N., Winter Park Memorial Hospital, Florida, examine a camel driver with the help of an Afghan interpreter.

Winter Park, Florida; and reporter Charles Thornton and photographer Peter Schlueter from the *Arizona Republic*, a newspaper in Phoenix.

They spent the first week getting used to the climate and food, buying the necessary medical supplies, and arranging for them to be carried by camel to their destination. The group then traveled to Quetta, a small town just across the border from Afghanistan, where they met the 15 bodyguards and interpreters who would accompany them.

Under cover of darkness, they slipped into Afghanistan, boarded a two-ton truck captured from the Russians and then began the 16-day journey across the country, traveling at night, then camouflaging the truck and sleeping by day.

They treated the sick at each stop, and were usually welcomed with open arms. Twice they were detained by Hazaras, a Shiite Muslim tribe aligned with Iran's Ayatollah Khomeini, but escaped by passing themselves off as Germans.

The journey was long and traveling was difficult since there were no roads. They finally arrived at the camp, a small village north of Kandahar, just one day ahead of their camels and supplies.

"There was no electricity, and our clinic was a grass hut. By dawn there would already be 15 to 20 people lined up outside," Dr. Jensen recalled. Working until dusk, they were able to treat about 40 patients a day.

Most common were the infectious diseases typical of underdeveloped countries: tuberculosis, measles, whooping cough, malaria, pneumonia, bronchitis, dysentery, otitis media, hepatitis and various skin infections.

Many suffered from scurvy and

B-vitamin deficiencies; protein and calorie malnutrition was prevalent in infants, Dr. Jensen said.

And then there were war injuries, which were as common among civilians as fighters.

Land mines and bomb "toys" shaped like butterflies caused innumerable hand and foot injuries, especially to children. "With immediate treatment, the injury could usually be repaired so that functional use of the limb was retained," Dr. Jensen explained. "Without it, gangrene or osteomyelitis set in and amputation was the only course left."

Dr. Jensen added, "Any serious wound in Afghanistan is ultimately fatal because of the lack of facilities and ability to transport. Anybody with an abdominal or chest wound dies."

The medical team was most effective treating the infectious and deficiency diseases. "We had lots of antibiotics with us and, if I handed out one vitamin, I handed out 20,000," Dr. Jensen said. "We also tried to give dietary instruction, but we were hampered by the cultural taboos against eating certain things, and the Afghans just didn't seem to understand the importance of different water sources for drinking, bathing and animal use."

After a week at the camp, the reporters were scheduled to return to Pakistan, and nurse John Moughan decided to return with them. But soon after they set out, tragedy struck.

"The jeep was ambushed by Soviets, and Charles was killed in the attack. Peter and John were separated, and John eventually made it back to where I was, with three wounded bodyguards. Peter made it back to Pakistan separately," Dr. Jensen said.

He and Moughan treated the wounded soldiers, then continued to operate the clinic for two more weeks. However, "the Soviets found Charles' body and his notes and, deciding there were more Americans in the area, began searching for us," Dr. Jensen said. The Afghans first moved the medical team to the mountains, then decided they should leave the country for their own safety.

"At dusk the second night out, we were driving over an open desert plateau when we were intercepted by two M124 helicopters. They fired on us with rockets and machine guns for about 20 minutes," Dr. Jensen recalled, shuddering.

Nightfall saved them and when helicopters attacked again the following night, they escaped by hiding in the trees of a narrow valley.

"Being shot at gives you a different perspective on life, what is important and what isn't. What you think about at the moment is what you'll miss if you die, and it isn't your BMW," Dr. Jensen declared.

The entire volunteer experience affected him deeply. "You get a very strong feeling for what an unusual place the United States is, in terms of its development, its economics, the health of its citizens," he explained. "We take our freedom for granted, that our destiny is in our own hands. It's generally not like that in the world."

Dr. Jensen said he probably won't go back to Afghanistan because "I've used up my luck," but he is considering doing additional medical service in a third-world country: "There's a lot to be gained from it. It's worth doing, it's satisfying, it's interesting, and it offers a lot of personal growth." K.H.

In The Philippines

It was usually dark by the time they arrived at a hospital. The dimly lit corridors, overrun with children at play, went quiet when they walked in. Two-hundred Asian eyes turned in unison to the tall, white strangers. They were anxious eyes. Terrified eyes. Curious eyes. Happy eyes. Hopeful eyes.

The American doctors had arrived.

Among these doctors who went to the Philippines was Craig Bradley, M.D., assistant professor and associate attending physician, plastic and reconstructive surgery.

Dr. Bradley traveled the 9,000 miles with 12 other surgeons, their wives, 3 anesthesiologists and 3 surgical nurses in order to repair as many cleft lips and palates as possible in 14 days.

The surgeons are all members of ICARUS, an international society of plastic surgeons. For the last few years ICARUS members have been taking such trips to the Philippines annually to train surgical residents and treat people in underserved communities. Modern medical facilities and trained personnel are available in Manila, but not on the outer islands.

"There's a high incidence of cleft lips and palates on these islands because they're genetic defects inbred among the natives," Dr. Bradley says. "But the medical facilities there can be 50 years out-of-date, if they exist; no plastic surgeons are available; and the people are

too poor to pay for medical help."

The group paid for their own expenses and donated their time, which, with traveling, amounted to a full month away from a practice at home. This was Dr. Bradley's first such expedition, and he was the only Chicago-area physician to make the trip.

The doctors spent two days operating in each of three towns: Iloilo on the island of Panay; Toledo, on

Cebu; and Balanga, on Luzon.

When they arrived at a hospital, they found children as young as a year old and adults who had lived with the facial deformities for 30 years waiting for help. Each community near the selected hospital had been allowed to send five people for the doctors to treat. Most of them were children.

"Just walking through the crowd to look at the patients was difficult



Craig Bradley, M.D., (left) operates on a Filipino child's cleft lip. His wife, Anne Bradley, R.N., and Ken Stern, M.D., from Louisville, Kentucky, assist.

because the families brought all their belongings with them," remembers Dr. Bradley. "And wherever you went, everyone's eyes followed you. You could tell some were afraid, but most were still really happy because they'd been selected. You'd think it was Christmas instead of an operation."

Unfortunately, getting to the hospital didn't guarantee they'd be treated. The first thing Dr. Bradley and the other surgeons did was choose the cases that were "doable."

"We couldn't help the people who needed a lot of post-op care," explains Dr. Bradley, "for instance, those who needed cranial-facial surgeries. We operated for two days and then moved on, and we had to be sure the patients would be OK after we left with the post-op care and facilities available."

With so little time and so many patients to help, the doctors had to be efficient. In all, they treated about 200 people; Dr. Bradley alone handled almost 30 cases during the six operating days.

During the same period of time here, he says he probably would have treated 18-20 patients.

"One reason we could handle so many cases was because our wives were there to help out as nurses, administrators, and operating room assistants," Dr. Bradley says. "We'd have one child at each end of an operating table, and when one was done, the wives would find a child to replace him. If the child on one end of the table was tall, they'd find a shorter child to fit the other end."

The average time between patients, therefore, was short. Minutes, in fact. The average time between patients in an O.R. here is 45 minutes to an hour.

"Of course, the O.R. procedures

weren't as formal there," notes Dr. Bradley. "The facilities on the whole were rather primitive in Iloilo and Balanga. The surgical instruments weren't sterilized, but soaked in antiseptic for five minutes, then reused. Fortunately, sterility is not terribly important with mouth surgery."

"Once I saw a native nurse trying to sterilize equipment with burning alcohol. She thought the more you let it burn, the more bacteria you'd kill, when actually that does no good at all. It's interesting that even with these compromises in sterility, the infection rate there is no higher than it is here for the same types of cases."

After operating on as many people as possible and checking on the patients afterwards, the group boarded a bus and headed to the airport for a commuter flight to the next island. But sometimes there was time for strolling through the villages and soaking up some local color.

"People would invite me and my wife Anne into their homes," says Dr. Bradley. "The thing that struck us most was that the people were so gracious, gentle and caring, in the middle of the worst poverty I've ever seen."

Dr. Bradley remembers shanty homes with cardboard sides and thatched roofs. Water, deadly dirty. An 18x20 foot house where eight people lived. Dirt floors.

But he also remembers children who followed them down the street, begging not for money but to have their picture taken. Homes that were meticulously clean. Parents who showed great affection for their children.

And he remembers the children he operated on, like eight-year-old Anthony, who lives with his nine

brothers and sisters in their 12 x 12 foot shack. After surgery, Dr. Bradley made rounds through the crowded, noisy wards. "Anthony," recalls Dr. Bradley, "through his swollen and repaired lips, was trying to smile at me."

"It just wasn't a depressing environment, despite the conditions. The people acknowledged they were poor, but their attitude was 'if things are going to get better, I have to work harder.' You didn't feel the negativism there that you do walking down the street in New York."

Something else Dr. Bradley found in the Philippines was a renewed sense of what he calls "the art of being a doctor."

"Medicine in the U.S. today involves politics and business. In the Philippines there were no insurance companies to fight with. No worrying about a litigious society. Nothing to deal with except the patients and their medical problems. Just to go out and practice your art was invigorating."

That freedom to concentrate on just the medical side of medicine is something Dr. Bradley will see again.

He and Anne plan to go back to the Philippines for what they hope will be an annual trip. J.P.

In Russia

What they both remember most were the eyes.

Dried yellowed hollows in faces tanned by radiation gave a "haunted look" to the patients they saw at Moscow Hospital. No. 6.

It was 39 days after the nuclear disaster at Chernobyl when Andrew Davis, M.D., assistant professor, internal and preventive medicine, and his wife, Lynn Dykstra, R.N., a staff member of the Medical Center, were among the first Americans to visit the Moscow hospital which was designated the radiation disaster treatment center.

"Our trip to the Soviet Union was an academic and cultural exchange planned long before the Chernobyl incident," says Dr. Davis, who is executive vice president of the Chicago Chapter of the Physicians for Social Responsibility.

"The idea was that if we have such exchanges, if we have our families and our colleagues there, we will understand each other better and nuclear war will be much less likely."

The 299 most affected by the Chernobyl explosion were sent to Moscow Hospital No. 6. Bed capacity at the hospital is about 350 so the influx of radiation victims nearly doubled the normal patient load. Within a few days, Dr. Davis said, staff was tripled so that radiation patients could be given undivided medical attention. "A CTA bus accident in Chicago," Dr. Davis adds, "would overwhelm just about any emergency room. A nuclear weapons explosion on a summer day when there are a lot of people outdoors, would affect about 300,000 people with serious radiation sickness. That would include doctors and nurses, too. Of course, some

hospitals would probably be destroyed as well."

Adds Dykstra, "Those kinds of figures make it clear that even with all our wonderful medical knowledge, there is no way we can medically handle nuclear war."

With the help of an interpreter, Dykstra talked for more than an hour to one of the Chernobyl patients—a 40-year-old turbine engineer whose blood tests showed he had 600 rads of radiation, calculated by chromosomal analysis and lymphocyte counts.

"More than 1,000 rads is fatal," Davis explains. "Between 400 and 1,000 is a gray zone, with survival depending on the kind of medical care available. Exposure measuring more than 100 rads is considered serious."

The turbine engineer, a five-foot, 10-inch tall man, was emaciated, weighing only 130 pounds. He had just started to get his appetite back. Visitors to his room had to wear gowns and masks, not for their own protection, but because the patient's immune system was suppressed so infection posed a serious threat.

He told Dykstra he was at the Chernobyl power plant as a consultant the day of the explosion and fire, April 26. He and a co-worker friend were checking vibrations in a turbine when they smelled something peculiar. They immediately went to the control room for oxygen masks and protective clothing and helped with the evacuation.

His friend got sick first, but within two hours of the explosion he also began feeling weak and nauseous. Then the vomiting, which he described as the "worst imaginable," began. It lasted four hours.

Nearly two weeks later, petichiae, the tiny bruises from radiation burns, appeared. His hair fell out.

Open wounds developed on the calves and hands; it was hard for him to understand, Dykstra said, how he could get first and second degree burns from radioactive dust that he didn't even notice at the accident site so many days before.

On day 14 he had a bone marrow transplant from his sister. It took. Then liver failure developed. Massive antibiotics were ordered. Anti-fungal agents continued to be prescribed for infections. His condition remained grave because of the hepatitis.

"He told me that he was very thankful for his care," Dykstra adds. "His doctor would only say that he 'wasn't doing well.' The look in his eyes, though, seemed to show that he knew he was dying." K.K.-K.

Medical Center Elects New Trustees

Four new Trustees and three Life Trustees were elected at the recent annual meeting of the Board of Trustees of Rush-Presbyterian-St. Luke's Medical Center.

New to the Board of Trustees are: Edward A. Brennan, Dino J. D'Angelo, Donald E. Nordlund and H. Blair White.

Brennan is chairman, chief executive officer, and a director of Sears, Roebuck and Co. A native of Chicago, he was graduated from Marquette University and joined Sears in 1956. In 1980 he was named president and, in January, 1986, chairman and chief executive officer. He is a director of the Sears Foundation, the National Retail Merchants Association and the American Retail Federation.

D'Angelo, a native of Italy, is an attorney, real estate developer and art collector who is credited with sparking the renaissance of Chicago's South Michigan Avenue. He received his B.A. and his J.D. degrees from The University of Chicago. In 1960 he helped establish the firm Fiffer & D'Angelo; later was a partner in the firm of Friedman & Koven, and, in 1981, started Lake Development Ltd., a real estate management company.

Nordlund is chairman, chief executive officer and a director of Staley Continental, Inc., a corn-refiner and food service distributor. He received his A.B. degree from Midland College in Texas and a J.D. degree from the University of Michigan. He joined Staley in 1956 and became chairman in 1975. He is a director of Amsted Industries, Inc., Sentry Insurance, Illinois Bell Telephone Company, Sundstrand Corporation, and Midwest Financial Group.

White is co-managing partner of the law firm of Sidley & Austin. He received his B.A. and J.D. degrees from the University of Iowa, and is a member of the American, Illinois



Edward A. Brennan



Dino J. D'Angelo



Donald E. Nordlund



H. Blair White

and Chicago bar associations, the American College of Trial Lawyers, and the Bar Association of the 7th Federal District. White is a director of DeKalb AgResearch, Inc., the Kimberly-Clark Corporation, and R.R. Donnelley & Sons, Inc.

The three Life Trustees elected are R. Gordon Brown, M.D., Robert J. Hasterlik, M.D., and E. Norman Staub.

Dr. Brown, a senior attending physician at the Medical Center and associate professor of medicine in Rush Medical College, was first elected a Trustee in 1970. A 1939 graduate of Rush Medical College, he and his family established the Ralph C. Brown, M.D., Chair of Internal Medicine at Rush to honor his father, also a Rush graduate.

Dr. Hasterlik, a graduate of Rush Medical College, was elected a Trustee in 1983. He was a professor of medicine at The University of Chicago and later at the University of Southern California. He now serves as a consultant to the National Cancer Institute, Scripps Memorial Hospital Cancer Center, and the State of Illinois Legislative Commission on Atomic Energy.

Staub was first elected a Trustee in 1974 and has been a member of the executive committee of the Trustees since 1981. He is a retired

chairman and chief executive officer of the Northern Trust Corporation and the Northern Trust Company and is also a director of the Wells Manufacturing Company.

Rush/Copley Hospital Announce Agreement

The leadership of Copley Memorial Hospital of Aurora and of Rush-Presbyterian-St. Luke's Medical Center announced in September an agreement to move ahead on a program to combine the two institutions.

The joint announcement from the Copley Board of Directors and the Executive Committee of the Trustees of the Medical Center said:

"Agreement has been reached in principle to consolidate the fiscal resources of our institutions to strengthen each of them. Copley will continue to operate as a community hospital with additional specialized resources for care from Rush-Presbyterian-St. Luke's."

The proposed arrangement would result in an exchange of Trustees between the two institutions, a study to determine the feasibility of construction of new patient care facilities to serve the suburban area west of Chicago, and provision of additional specialized services to the population currently served by Copley.

"The Copley Board of Directors believes that one of the primary benefits in joining with Rush-Presbyterian-St. Luke's is that we will be working together with a Medical Center that has both a regional and national reputation for high quality, cost effective health care," said D. Chet McKee, chairman of the Board at Copley.

Greg Lintjer, president of Copley, said, "This agreement is the beginning of an exciting new era for Copley. It will allow Copley the autonomy it needs to respond to our current service population while at the same time allowing us

to grow and expand to meet the challenges of delivering health care to the residents of Aurora and other western suburbs."

Leo M. Henikoff, M.D., president of Rush-Presbyterian-St. Luke's, stressed that while the management and the medical staff of each institution will maintain their independence, "the new corporate structure will enable Rush to offer certain resources usually not available to Copley's excellent community based care programs.

"The union of two successful institutions, an academic medical center and an excellent community hospital, creates a more stable financial and patient care base for each in a period of rapidly changing health care," Dr. Henikoff said. "We are pleased to share a common vision of service with such a vigorous institution as Copley."

Both organizations will now develop the final contractual documents that will legally define the new relationship. These documents will be reviewed by the boards of each institution, with further approval expected by early 1987.

Under the proposed agreement, two Copley Board members will join the Rush Board as Trustees. These Board members will represent Copley on Rush-Presbyterian-St. Luke's Executive and other Board committees.

Two Rush-Presbyterian-St. Luke's Board members will be added to the Copley Memorial Board and Copley's parent board, the Fox Valley Health Services Corporation.

The arrangement provides for the creation of a Copley/Rush parent board that would have certain reserve powers; for instance, the review and approval of the annual strategic plan and selection of auditors.

The Copley Board will continue to hire its hospital president and administrative staff. The management of patient care at Copley will remain the responsibility of Copley's medical staff.

Founded in 1886, Copley is a 319-bed acute care community hospital in Aurora, Illinois. In addition to a full range of medical, surgical, pediatric and obstetrics services, the hospital offers special care in other areas through the Copley Heart Center and the Copley Cancer Care Center.

Rush Adds Six Endowed Professors

Six Rush-Presbyterian-St. Luke's Medical Center physicians were named to endowed professorships by the Board of Trustees in 1986. The appointments include a new chair in orthopedic surgery and established chairs in pediatrics, hematology, internal medicine, gastroenterology and rheumatology. The Medical Center's new named professors are:

**Jorge O. Galante, M.D., D.M.Sc.,
the William A. Hark, M.D. —
Susanne G. Swift Professor
of Orthopedic Surgery**

Dr. Galante, professor and chairman, Department of Orthopedic Surgery at the Medical Center since 1972, is recognized as a pioneer of hip joint replacement surgery and a leader in cementless joint replacements.

Born in Buenos Aires, Argentina, Dr. Galante earned his B.A. degree at the Colegio Nacional de Buenos Aires and his M.D. at the University of Buenos Aires Medical School. He served as associate investigator in the bioengineering laboratory and as associate professor of orthopedics at the University of Goteborg, Sweden, where he received a D.M.Sc. degree. Dr. Galante completed his residency in orthopedic surgery at Michael Reese Hospital and Medical Center and a residency and research fellowship at the University of Illinois Research and Education Hospitals.

Among Dr. Galante's many honors and awards are: the highest

scholastic standing at the University of Buenos Aires, the Kappa Delta Award for outstanding research in orthopedic surgery and the Clemson University Award for outstanding contributions to applied research in biomaterials.

Dr. Galante is widely published and is a member of numerous medical societies. He is president-elect of the Chicago Orthopedic Society, immediate past president of the HIP Society and former president and current trustee of the Orthopedic Research and Education Foundation.

The Hark/Swift chair is named for the late William A. Hark, M.D., a former member of the Department of Orthopedic Surgery, and Susanne G. Swift, a patient of Dr. Hark and his father, Fred W. Hark, M.D. Members of the orthopedic surgery department, family and friends of Dr. Hark and Ms. Swift and Dr. Hark's patients contributed funds to the endowed chair.

**Samuel P. Gotoff, M.D.,
the Woman's Board Professor
of Pediatrics**

Dr. Gotoff, holder of the country's first endowed hospital chair of pediatrics, is a professor and the chairman of pediatrics at Rush-Presbyterian-St. Luke's Medical Center. He joined the Medical Center staff in 1986 after more than ten years as chairman of pediatrics at Michael Reese Hospital and Medical Center and professor of pediatrics at the Pritzker School of Medicine of The University of Chicago.

Dr. Gotoff, a consultant on infectious diseases and immunologic disorders in children, is internationally known for epidemiologic and immunologic studies on group B streptococcus. He is studying this major bacterium, responsible for serious infection in newborn infants, under grants from the National Institutes of Health. He has published more than 80 scientific articles and has edited the *Journal of Infectious Diseases and Infection*.

Rush Rounds

A native of New York City, Dr. Gotoff earned his bachelor's degree at Amherst College in Massachusetts and his M.D. degree from the University of Rochester School of Medicine, Rochester, New York. He is board-certified in pediatrics and allergy/immunology, is a member of the executive committee of the Chicago Pediatric Society and is a former member of the Committee on Infectious Diseases, American Academy of Pediatrics.

Dr. Gotoff is a member of numerous academic and professional societies and has trained more than 200 pediatric residents, many of whom are practicing in the Chicago area.

William H. Knospe, M.D., the Elodia Kehm Professor of Hematology

Dr. Knospe is director of the Section of Hematology at Rush-Presbyterian-St. Luke's Medical Center, a senior attending physician in internal medicine and professor of medicine at Rush Medical College. He came to the Medical Center in 1967 as assistant director of hematology for the radio-hematology laboratory and later directed the Section of Clinical Hematology.

Dr. Knospe, who received B.A. and B.S. degrees from the University of Illinois, earned his M.D. from the University of Illinois School of Medicine and his M.S. in radiation biology from the University of Rochester School of Medicine, Rochester, New York. He served the U.S. Army as chief of medical services at the U.S. Army Hospital in Berlin, West Germany, and as an investigator and chief of the hematology clinic at Walter Reed Army Medical Center, Washington, D.C.

A member of the Medical Center's Thomas Hazen Thorne Bone Marrow Transplant Center, Dr. Knospe's current work includes the clinical aspects of leukemia and other blood malignancies.

He sits on the board of trustees

of the Leukemia Society of America, Inc., Illinois chapter, and has lectured around the world in such locations as Brazil, Japan and China. He has published more than 80 papers.

The Elodia Kehm Chair of Hematology was established in 1969 by a bequest honoring Elodia Kehm, widow of the owner of Kehm Construction, who died of cancer in 1932.

Stuart Levin, M.D., the James Lowenstine Professor of Internal Medicine

Dr. Levin is director of the Section of Infectious Disease and associate chairman of the Department of Medicine. He holds academic positions in three Rush Medical College departments: medicine, as a professor, and preventive medicine and immunology/microbiology, as associate professor. He is also a senior attending physician in medicine and preventive medicine and senior scientist in microbiology.

A medical school graduate of the University of Illinois, Dr. Levin completed a rotating internship at Cook County Hospital and a residency in internal medicine at the West Side Veterans Hospital. He then served as assistant chief of medicine and chief of infectious disease at the General Leonard Wood Army Hospital in Fort Wood, Missouri, before coming to the Medical Center on a fellowship in 1966. While at the Medical Center, Dr. Levin has been a consultant in infectious disease to the Chicago Board of Health.

Dr. Levin is editor of the *Journal of Nosocomial Infections*, and associate editor of *Infections in Medicine* and the *AMA Archives of Internal Medicine*. He holds memberships in numerous medical societies, has been honored with teaching awards from four institutions and has published more than 50 articles.

The James Lowenstine Chair of Internal Medicine, created in 1971 by the Lowenstine Foundation, honors the late president of the

Central Steel and Wire Company and promotes the clinical training of the family doctor.

Seymour M. Sabesin, M.D., the Josephine Dyrenforth Professor of Gastroenterology

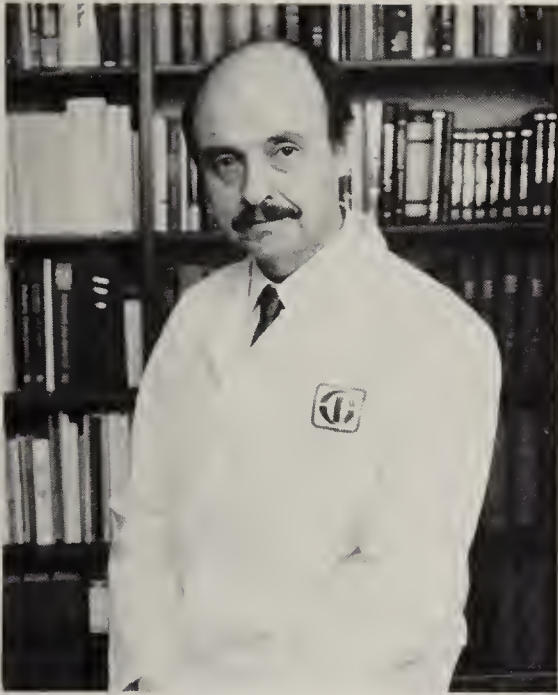
Dr. Sabesin is director of the Section of Digestive Diseases, as well as professor and senior attending in the Department of Internal Medicine. He came to the Medical Center in 1985, from the University of Tennessee where he had been professor of medicine and director of the division of gastroenterology since 1973.

Dr. Sabesin is a graduate of the City College of New York and the New York University School of Medicine, which awarded him an M.D. degree in 1958. His residency was completed at Cornell Hospital in New York.

Dr. Sabesin's studies in hepatic lipoprotein metabolism, particularly in alcoholic liver disease, are recognized as classics in the field. His current research includes the role of the liver in lipoprotein metabolism, ultrastructural and biochemical studies of lipoprotein transport by the intestine and liver, and experimental liver injury. He is also principal and co-principal investigator on five studies funded by the National Institutes of Health.

As part of the Medical Center's liver transplant team, Dr. Sabesin assists transplant surgeons with pre-surgical evaluations and post-surgical care. He is internationally recognized for his 90-plus publications. He holds memberships in numerous medical and professional societies and on the editorial boards of the *American Journal of Physiology*, *Gastroenterology*, *Hepatology* and *Current Concept in Gastroenterology*.

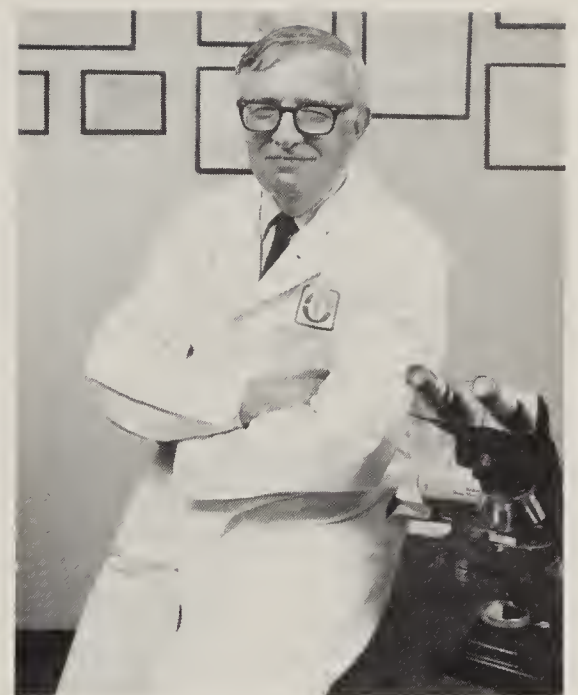
The Josephine Dyrenforth Chair of Gastroenterology was established in 1968 by Mrs. Dyrenforth in appreciation of the care given her husband, Arthur, a prominent Chicago attorney.



Jorge O. Galante, M.D.



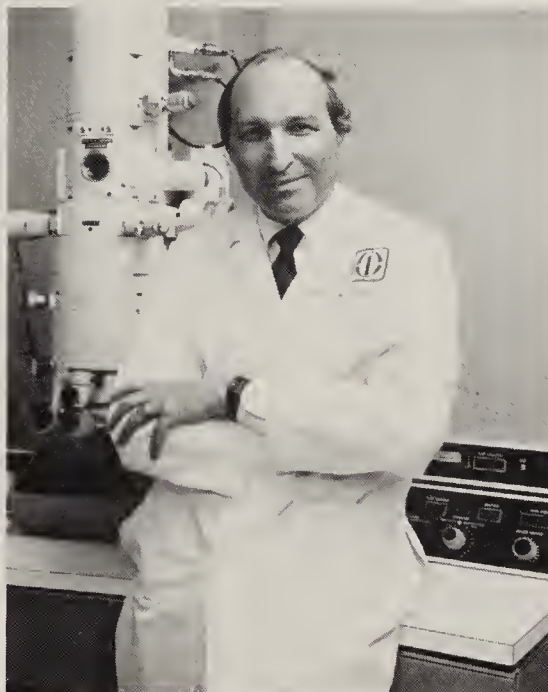
Samuel P. Gotoff, M.D.



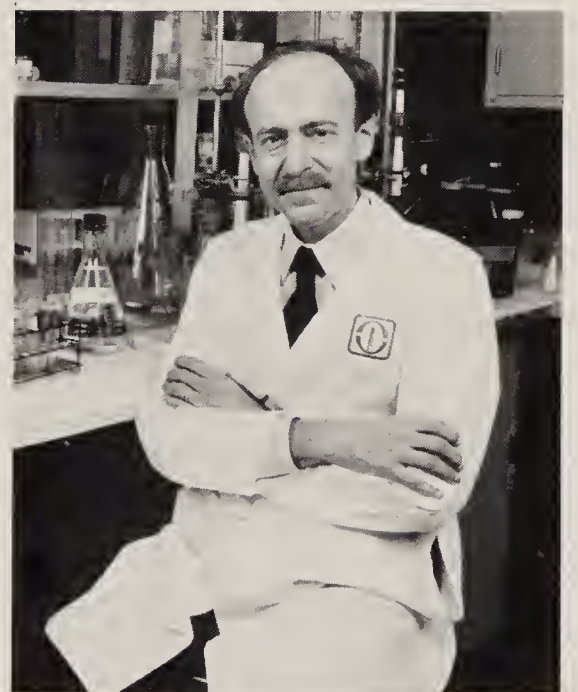
William H. Knospe, M.D.



Stuart Levin, M.D.



Seymour M. Sabesin, M.D.



Thomas J. Schnitzer, M.D., Ph.D.

**Thomas J. Schnitzer, M.D., Ph.D.,
the Willard W. Wood, M.D.,
Professor of Rheumatology**

Dr. Schnitzer is chief of the Section of Rheumatology and Geriatrics, professor of medicine and senior attending physician at Rush-Presbyterian-St. Luke's Medical Center. He came to the Medical Center in 1985 after six years at the University of Michigan School of Public Health and the University of Michigan Medical School, both in Ann Arbor, Michigan.

Born in Czechoslovakia, Dr. Schnitzer earned his B.A. degree in biochemistry from Princeton Uni-

versity, summa cum laude. He obtained his M.D. degree from Harvard Medical School, cum laude, completed his residency at Johns Hopkins Hospital, Baltimore, Maryland, trained as a research associate for the National Institutes of Health, National Institute of Allergy and Infectious Disease, Bethesda, Maryland, and completed a fellowship in the Medical Research Council Rheumatism Unit in England.

Dr. Schnitzer, whose research focuses primarily on arthritis, was honored with the Senior Investigator Award from the Arthritis Foun-

dation. While at the University of Michigan, he coordinated the clinical teaching conferences of the Arthritis Division, Department of Medicine. He has published more than 30 papers and contributed to several medical textbooks.

The Willard W. Wood, M.D., Chair of Rheumatology was established in 1969 by Charles S. Pillsbury, his family and other patients of Dr. Wood. Dr. Wood was a Rush Medical College graduate and a faculty member at the Medical Center for more than 55 years.

J.F.

RushRounds

Rush Establishes Children's Service

Measles . . . mumps . . . scraped knees and elbows—the familiar lumps, bumps and ailments of childhood. But children also suffer from serious conditions usually associated with adulthood. Some have kidney diseases so advanced they need a kidney transplant. The majority of bone cancer victims are between the ages of 10 and 20. Mental health researchers are finding childhood depression surprisingly widespread. Even a toddler can get a migraine.

To respond to this wide range of problems in infants, children, and adolescents, Rush-Presbyterian-St. Luke's Medical Center has established The Children's Service. Said Samuel P. Gotoff, M.D., the Woman's Board professor and chairman of pediatrics: "The Service will put all the specialties and programs for children within the departments of pediatrics, surgery and psychiatry within easy reach of young patients, their parents and the referring physician."

The Service includes several new pediatric programs and specialists.

The Midwest Pediatric Kidney Disease Center: This center, under the direction of Eddie S. Moore, M.D., includes the Pediatric Chronic Renal Failure Program. This program's aim is to take children off dialysis with a kidney transplant. Dr. Moore, with colleague Jonathan D. Heiliczer, M.D., prepare children and their parents for an eventual transplant by surgeons in the Medical Center's Section of Transplantation.

"The most common reasons for a child to need dialysis are congenital kidney problems, including structural abnormalities and blockage," says Dr. Moore. Allergic conditions and post-infection problems can also severely affect the kidneys and warrant intensive treatment.



Peter Heydemann, M.D., director, Section of Pediatric Neurology, examines a young patient.

Although the Medical Center has offered acute dialysis treatments for children for many years, this is the first time a multidisciplinary chronic renal failure program has been available for pediatric patients.

"Most of our children need three four-hour treatments weekly," Dr. Moore says. When the program is completely in place, he hopes that a child's time in the dialysis unit will be broken into four hourly sessions that include schoolwork with a teacher from the Chicago Board of Education, therapeutic activities with the Medical Center's child life coordinators, patient teaching programs with the unit's nursing staff, and free time to watch television, do homework or just relax.

Other components of the Midwest Pediatric Kidney Disease Center include in-depth consultation and multidisciplinary treatment services for children with kidney disorders; professional education programs for physicians, residents and medical students; and an extensive research program. Two National Institutes of Health grants support projects in developmental renal physiology and a nationwide multicenter study on impeded

growth in children with chronic renal disease.

Behavioral Pediatrics Program: Anthony Richtsmeier, M.D., director of the Section of Behavioral Pediatrics, uses his training in pediatrics and child psychiatry to help children, adolescents and their families deal with a variety of physical, psychological, developmental, social and environmental problems. "One of my major research interests," he notes, "is the total impact of physical illnesses on children and their families."

"Usually, a number of psychological factors need to be considered when evaluating these children and their families. Even common pediatrics problems, such as bed-wetting and recurrent pains, can be complicated and require expertise in both the physical and psychological aspects of these disorders."

Dr. Richtsmeier is also developing a new Behavioral Pediatrics Program for outpatients, which will provide consultation and short-term intervention services. Patients currently in the program are being helped with recurrent pain; school problems (underachievement, avoidance); problem behaviors (dis-

RushRounds

cipline problems, hyperactivity); adjustment difficulties (divorce, death, illness, adoption, traumatic events); developmental problems; and problems interacting with other family members.

Section of Pediatric Neurology: "A careful, complete history can go a long way in helping a neurologist determine a specific diagnosis," says Peter Heydemann, M.D., director of the Section of Pediatric Neurology. Using epilepsy to illustrate his point, Dr. Heydemann says that only several children in a thousand have true epileptic seizures, although many children and adolescents are diagnosed as having this disorder.

"In infants, these pseudo-seizures can be initiated by long crying spells," he explains. "By researching this phenomenon we discovered that, in comforting their child, parents would pick up the baby, rest the infant's head on their shoulder and, in the process, aggravate the spell. We found if the parent picks up the baby and holds the infant horizontally, the spell goes away much more quickly."

Teens can also have episodes that mimic seizures, in the form of anxiety/panic attacks. These "seizures" are marked by breathing heavily, feeling dazed, and having dizzy spells and blackouts.

"Anti-convulsants won't help these adolescents," Dr. Heydemann points out. "But recognizing the events that precipitate the spells and dealing with their underlying anxieties usually help ward off these pseudo-seizures."

Headaches, especially tension/stress and migraine, are also common neurological problems in children. To control the onset of migraines, Dr. Heydemann is currently studying the effects of restricting certain types of food, including chocolate, nuts, and cheese.

"We still can't cure migraine headaches, but we hope to lessen the severity and frequency of the epi-

sodes and help children adapt to this condition," he says.

Section of Pediatric Infectious Disease: According to Kenneth Boyer, M.D., director of the Section of Pediatric Infectious Disease, one of the most common reasons children go to a pediatrician is for an infectious disease problem.

To illustrate the variety of cases he consults on, Dr. Boyer described some of his recent patients: a pregnant 15-year-old with measles; a six-year-old boy with short bowel syndrome infected from a hyperalimentation line being used to feed him; and a three-year-old girl who caught AIDS from her mother.

Dr. Boyer's research on group B streptococcal infection centers on one of the most common life-threatening problems in newborns.

"The infant mortality rate in the United States is 10 to 15 per 1000 live births," he says. "The majority of these deaths are due to prematurity. But two to ten percent of them, depending on the baby's size, are caused by group B streptococcal infection."

For the past eight years, Drs. Boyer and Gotoff have been involved in National Institutes of Health-funded studies to determine if these deaths can be prevented. Dr. Boyer has developed a method of preventing the infections by the use of antibodies during labor and delivery; Dr. Gotoff developed methods to determine why some babies are susceptible to group B strep infections and others are not.

"We hope that our studies will ultimately lead to screening for strep during pregnancy and possibly to the development of a vaccine," Dr. Boyer says. M.A.R.

Dr. Harris Heads Rush Cancer Center

Jules E. Harris, M.D., senior attending physician, internal medicine, has been appointed director of the Rush Cancer Center. He succeeds C. Frederick Kittle, M.D.,



Jules E. Harris, M.D., director, Rush Cancer Center.

senior attending surgeon, cardiovascular-thoracic surgery, who had served as acting director.

Dr. Harris, the Samuel G. Taylor III, professor of medicine, professor of immunology/microbiology and director of the Section of Medical Oncology, has been a member of the Medical Center's staff for eight years. He is also associate director for clinical trials of the Illinois Cancer Council—the comprehensive cancer center for the State of Illinois.

Known as a researcher in tumor immunology, Dr. Harris is widely published and serves on numerous review boards. He is the immediate past chairman of the Medical Advisory Board of the Leukemia Research Foundation.

The Rush Cancer Center was established in the mid-seventies to bring together disciplines relating to cancer care. Today the Medical Center is a referral center for patients with cancer of all kinds.

Recently Dr. Harris also received another honor. On September 30, the Jules E. Harris Chair in Oncology at Ben-Gurion University of the Negev in Beer-Sheva, Israel, was dedicated in a ceremony held in Chicago. The chair was funded by

Rush Rounds

the family of Judd and Marjorie Weinberg of Winnetka.

The first holder of the chair is Yoram Cohen, M.D., who is currently on the medical staff at Ben-Gurion University. Dr. Cohen attended the dedication ceremony, and while in Chicago lectured at Rush University as a visiting professor.

Dr. Harris has been active for a number of years in assisting with the growth and development of the medical school at Ben Gurion University. He is at present a member of the university's international Board of Governors and has organized an exchange program within Rush Medical College for medical students from Ben Gurion University. J.P.

Rush Services Span Chicago Area

Rush-Presbyterian-St. Luke's continued its expansion of special services and outreach facilities during 1986. New additions were a preferred provider organization (PPO), health care and fitness centers in two new major complexes in Chicago's downtown, and occupational health facilities in expanding industrial areas in the city's suburbs.

Rush Contract Care, the recently launched PPO, is a new type of health care service for businesses that substantially cuts the cost of employees' health care benefits.

"In essence, we are a pre-purchaser of physician services and hospital beds, supplies and services," explains Gordon Mallett, M.H.S.A., director, Rush Contract Care. "The member physicians and hospitals agree to accept a limit on their charges, which represent savings to the patient."

In addition, many PPOs are available only through one insurance carrier. Rush Contract Care can be added onto a plan already in use by the employer. The insurance carrier need not be changed, points out Jerome J. Hahn, M.D., medical

director of Rush Contract Care and of the Medical Center's Sheridan Road Hospital.

As of fall, 1986, 16 Chicago area hospitals and more than 900 physicians operating out of 1,000 office locations had affiliated with Rush Contract Care.

Under a PPO, the employee/patient is free to use whichever doctor and hospital he or she chooses. If that doctor and hospital are part of the PPO network, most and sometimes all of the cost is covered by insurance. If the doctor and hospital are not part of the network, the employee/patient is usually responsible for a larger portion of the bill.

To provide sports medicine, preventive medicine, wellness and general health care to residents and workers in Chicago's South Loop and the city's downtown Dearborn and Burnham Park areas, the Medical Center leased 11,000 square feet in River City, a mixed-use residential and commercial development on the East bank of the Chicago River.

About 8,000 square feet is occupied by Orthopedic Associates, whose members are all on the staff of the Medical Center. They provide sports medicine, occupational orthopedics, and oncologic, pediatric, arthritic, total joint, and general orthopedic services at the River City location.

The remainder of the space is dedicated to the River City Medical Center. Here, Michael Davidson, M.D., adjunct attending physician, offers a variety of fitness and preventive medicine programs as well as a traditional internal medicine practice. In addition to serving businesses and individuals in the area, the River City Medical Center provides physicals and other services to members of the adjacent City Club at River City, a health and fitness center.

Rush-Presbyterian-St. Luke's also has leased 50,000 square feet in the Northwestern Atrium Build-

ing, a new complex just being completed on the west side of the Loop. The facility planned for this building includes physicians' offices, a pharmacy, fitness center, cardiac rehabilitation program and other health care services. The building, which houses the Northwestern Railroad's downtown station, is visited by 60,000 commuters daily. The Rush facility will be easily accessible to commuters as well as the 6,000 employees who will work in the building and the 4,000 residents of nearby Presidential Towers, a new multi-story apartment complex.

Two new occupational health centers have also been added to the Rush Occupational Health Network, bringing the network's total to six. The two clinics, located in the northwestern part of the Chicago metropolitan area, are in one of the fastest growing areas for heavy and service industries, according to Dr. Hahn, who is also medical director of Diversified Health Services, which oversees the clinics.

The occupational health centers are specifically designed for employees of industrial firms. They provide medical treatment for work-related injuries and illnesses as well as physical examinations, diagnostic services, physical therapy, disability evaluations and health records maintenance.

This health network will continue to grow, Dr. Hahn adds. "We're evaluating several additional sites and hope to bring our services to the south side of Chicago in the next year." K.H.

IVF Program Greeted First Set of Twins

When Kevin Michael and Andrew John were born at the Medical Center in 1986, their birth marked two firsts for the Medical Center's In Vitro Fertilization (IVF) Program.

The boys are believed to be the



Mrs. Dale Martin and son, Matthew, introduce Illinois' first in vitro twins, Kevin Michael and Andrew John.

first set of IVF twins conceived through and delivered by an Illinois IVF program. The babies were born one minute apart—at 8:51 and 8:52—by cesarean section. They weighed in at 7 lbs., and 7 lbs. 14 oz.

The parents, Dale and Janice Martin of Batavia, a suburb of Chicago, enrolled in the Rush IVF program in June, 1984. The first IVF procedure was performed on Mrs. Martin in January, 1985. This was not a success because the eggs did not mature or fertilize.

In October of 1985, the 28-year-old woman underwent a second IVF procedure performed by W. Paul Dmowski, M.D., Ph.D., professor and senior attending physician, obstetrics and gynecology, and director of the Rush IVF program. This time the procedure resulted in a pregnancy, and the Martins, parents of a seven-and-a-half-year-old son, Matthew, learned their family was to increase by two! The delivery was performed by Donna Kirz, M.D., assistant professor and assistant attending physician, obstetrics and gynecology.

The Rush IVF program, opened in October, 1983, has treated 93

women. Results, to date, are eleven clinical pregnancies. The program's first live birth, a girl, was announced in March, 1985. The second birth, a boy, was in February, 1986. Two women are currently expecting babies.

G.S.

Staple Gun Fuses Bones

Broken bones can now be held together by staples until they heal, thanks to the invention of Jules S. Shapiro, M.D., associate professor and associate attending surgeon, orthopedic surgery. Use of this staple gun in more than 1,000 patients around the world confirms Dr. Shapiro's finding that the new stapling technique is faster than existing methods of attaching bones to one another and also is often stronger.

The idea for the Shapiro Staple Gun was conceived as Dr. Shapiro walked through the exhibit hall of an orthopedic convention in New Orleans five years ago. He stopped at the 3M Company's booth to watch a demonstration of a skin stapler, a device for closing incisions after surgery. Afterwards, he asked if the company made a bone stapler, too. "No," he was told, "but that's a good idea."

Of course, there was a long road from idea to finished product. One of Dr. Shapiro's first steps was to learn why surgeons did not more often use bone staples the old-fashioned way.

Different kinds of metal staples have been used by orthopedic surgeons for many years. But their uses have been limited by the technique for driving them in. "No self-respecting carpenter would drive staples like that," Dr. Shapiro said. The old way of doing it was to hold the staple with a clamp in one hand while the other hand pounded it in with a hammer. Besides being cumbersome, the technique was slow

and inefficient and often resulted in a poor attachment.

First, Dr. Shapiro tested his idea by using a carpenter's staple gun on the bones of cadavers. Then he consulted with 3M engineers who worked closely with him in the development of his gun. They suggested that its driving force should be compressed air rather than a spring so that a staple could be hammered more than once. Compressed air is readily available in operating rooms, either through wall outlets or tanks.

Another important element of its design was its shape, like that of a pistol, in order to allow the surgeon to place the staple accurately. The gun has two triggers: one loads the staple, the other trigger fires it off. "Unlike a firearm," Dr. Shapiro explains, "you don't squeeze this trigger, you jerk it, because that gives the staple maximum force."

He calls his invention the Shapiro Internal Fixation System because it sets bones from inside the body, rather than from outside, as a plaster cast does. The new staple gun is only the first salvo in a whole new attack on the orthopedic problem of attaching bone to bone, and other things to bone, Dr. Shapiro says.

Approved by the U.S. Food and Drug Administration three years ago, the Shapiro staple gun operates on the same principle as staple guns used by do-it-yourselfers and carpenters: driven by the force of the gun, the two legs of the staple are held fast by the compressive force of the solid substance they penetrate. In carpentry, the substance is likely to be wallboard; in orthopedic surgery the substance is metaphyseal bone which is like wallboard in that its surface is hard and its core spongy. Joints of fingers, toes, arms and legs are examples of metaphyseal bone.

While the surgical bone staples look much like carpentry staples, they are made of titanium which doesn't provoke body reactions,

rather than steel, which does. Dr. Shapiro says the flexibility of their use allows them not only to hold together fractured bones but also to hold together bones from which a segment has been removed, as in surgery for cancer or arthritis. The staples can also attach ligaments and tendons to bone and have been successfully used to hold together halves of rib cages which were sawed apart in order to perform open-chest surgery.

In each application, Dr. Shapiro explains, the staples can be used alone or in conjunction with such other fastening devices as sutures or plates and screws.

Dr. Shapiro's staple gun is graceful, quick, efficient, and produces firm attachment. "I repaired a badly broken ankle in 24 minutes," he explains. "And I was able to fuse a hammertoe on an outpatient basis with the staple gun." He sees the new invention as helping free time in the overtaxed schedules of operating rooms.

Another advantage of the staple is its lightness. "Because it has essentially no mass, the staple can stay in for life, unlike plates and screws which eventually have to be removed," he says.

Thus far the staple gun has been applied in more than 300 operations of patients at Rush-Presbyterian-St. Luke's Medical Center and in more than 700 patients in other countries including Germany, Sweden, and the United Kingdom. Among the foreign cases are more than 150 in Switzerland, whose orthopedic surgeons have led the world in internal fixation. "Now," Dr. Shapiro says, "they are using my gun."

The highly successful staple gun has produced a complication rate of only 4 percent.

The Shapiro Bone Stapler is being manufactured by the 3M Company and sold under the trade name Staplizer.

T.B.

Lennette Named Distinguished Alumnus

The Alumni Association of Rush Medical College this year awarded its highest honor to Edwin H. Lennette, M.D., Ph.D., Class of 1936.

The 1986 Distinguished Alumnus was recognized at the traditional Rush Medical College commencement banquet where he was introduced as a "world class microbiologist" and a "major force in the establishment of public health virology."

After graduation from Rush, Dr. Lennette taught and did research in Chicago before he joined the international health division of the Rockefeller Foundation where his assignments included influenza studies and yellow fever research in Brazil.

In 1947 he joined the California Department of Health Services as chief of its Viral and Rickettsial Disease Laboratory which he headed for 31 years. Under his direction it was considered the best in the country, having developed specific diagnostic tests for viruses difficult to diagnose and identify. Over the years, Dr. Lennette also headed the department's cancer research program and the laboratory and biomedical programs. His work in maintaining high evaluation standards for vaccines has been instrumental in the prevention of poliomyelitis and rubella.

Dr. Lennette has been recognized with many professional honors, including the American Public Health Association's Bronfman Award and the Wyeth Award in Clinical Microbiology. In accepting the distinguished alumnus award from Rush, he reflected on what has happened in his field over the past 50 years.

"When I entered the field of virology, there was not even a textbook. We didn't even know what we were working with. We couldn't see anything until the electron microscope and even the first of these would



Edwin Lennette, M.D., 1986 Distinguished Alumnus, Rush Medical College.

permit magnifications of about 20,000 diameters, and that's about all it did. There was no increase in resolution, so we saw a big item but we couldn't resolve what the structure was.

"We've gone a long way. As a matter of fact, we have come to the stage now where (we know that) viruses are involved not only in infectious disease processes, but also in neurological diseases as well as in cancer and in autoimmune diseases.

"So the whole area is opened up and this is a big difference from the 1930s when, if you didn't know the causation of the disease, you automatically put it in this waste basket known as 'viruses'."

Semi-retired since 1978, Dr. Lennette is president of the California Public Health Foundation and of the board of directors of the Paralta Cancer Research Institute in Oakland, California.

He is the author of more than 350 scientific publications, including books, serves on the editorial board of five journals, and is active in a number of medical societies. He has also recently been appointed president of the U.S. subsidiary of Virion Corporation. KK-K.

New Program Focuses On Family Violence

Often they come to the emergency services department at night. They are wounded physically and emotionally. They are frightened, desperate and distrustful.

"They" are the victims of domestic, or family violence. Each year, about 10 million Americans suffer some kind of abuse in the home. Children, wives and the elderly seek emergency treatment for a variety of injuries. Every month the Medical Center's emergency services department, treats some 20 child abuse and neglect victims, 30 abused wives, five sexual assault victims and two cases of elderly abuse or neglect.

The Rush-Presbyterian-St. Luke's Medical Center Departments of Medical Nursing, Social Services and Emergency Services have responded to the serious health problems and issues affecting victims of family violence with the formation of the Family Violence Program. It is the only such hospital-based program in Illinois designed to intervene, assess, educate and refer abuse victims to appropriate support and other services specifically set up to help them survive and cope.

In addition to abuse victims who come to Emergency Services for treatment, employees of the Medical Center, patients referred by private physicians, employees from local businesses, schools, church groups, social service and community welfare agencies and groups, can call the program's 24-hour line—(312) 94-ABUSE—and receive assistance.

"The health professional an abuse victim talks to may be the first person outside of the home to discover a long pattern of abuse and neglect. What they do, or don't do to assist the victim, at that critical time can have long-term health effects," says Daniel J. Sheridan, M.S., R.N., coordinator, Family

Violence Program.

In addition to aiding victims, the Family Violence Program is reaching out to Rush University nursing and medical students through lectures on the nature and treatment of abuse. Sheridan and fellow program staffer Linda Belknap R.N., also lead educational and awareness workshops and seminars on abuse and family violence for West Side community residents, PTAs, church groups, other hospital emergency services departments and schools.

A weekly support group for battered women has also been introduced. It is led by Belknap and a staff member from Rainbow House, a local shelter. In the group meetings, held on the Medical Center campus, women can talk about their feelings, gain self-worth, exchange information and learn that they have choices about their lives.

Sheridan stresses, "We believe that we can help stem the epidemic wave of abuse and its deleterious health effects on the family."

The Medical Center and program director Sheridan have been involved in the problem of family violence for some years. As a Rush University nursing student, Sheridan served as a volunteer for a 24-hour family crisis hotline on Chicago's South Side. As a junior nursing student in 1980, he initiated the organization of the Rush Coalition against Spouse Abuse (RCASA), which evolved into a Medical Center-wide employee volunteer group. Among the group's accomplishments was the printing and distribution of over 50,000 cards with numbers to call for help for domestic violence victims, where to refer battered women for emergency lodging and where men who abuse could call for counseling.

The cards are still used by Medical Center staff and by community residents and groups as a resource for major social service agencies in Chicago that assist domestic violence victims in ways not usually

available in most health care institutions.

In addition to the cards, RCASA members produced a one-minute television spot for Rush's patient information network, held hundreds of in-service workshops and seminars for Medical Center staff and community groups and agencies, contacted other emergency services departments and physicians' groups about family violence to advise of existing resources for victims.

In 1981, Rush-Presbyterian-St. Luke's Medical Center became a member of the Chicago Metropolitan Battered Women's Network. Sheridan currently serves as the chairman of the Network's health committee.

Sheridan also secured support from the Metropolitan Chicago Healthcare Council for producing a book of guidelines. The work—"Guidelines for the Treatment of Battered Women Victims in the Emergency Room Setting"—was co-authored by Sheridan and four others, including Belknap.

It assists nurses, doctors, other health care professionals and clerical staff in following the detailed procedures designed to aid and protect the individual as well as offering other help, such as individual and family counseling. The guidelines are included in Rush's emergency services department's policy and procedures handbook. C.E

Nursing Students Adopt Grandparents

"My grandma knows so much about the city of Chicago and its history. She teaches me a lot. I teach her about modern things, like her new microwave oven. When she first got it, she didn't know how to use it. We learn from each other."

Sounds like a typical warm family relationship, right? Except that the "granddaughter" is Cindy Biese, a senior nursing student in Rush University, and the "grandmother"

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is Julia Guillory, who lives in the apartments at the Medical Center's Johnston R. Bowman Health Center for the Elderly. Both are participants in the University's Student Nurses Association's "Adopt-A-Grandparent" program.

"We started the program to fulfill the community service function of the nursing association. Since many of the people who live in JRB don't have family nearby, they get lonesome," says student Janet Detato, SNA president and program founder. "It's turned out to be really enjoyable for everyone. The students are finding out there's no such thing as a generation gap."

Detato and co-coordinator Anne Donnelly first surveyed the apartment dwellers in JRB to find out who wanted to participate. Both "grandmas" and "granddaughters" filled out interest cards so they could be matched on the basis of common hobbies and activities.

Since the program started, seven JRB residents have been matched with pairs of granddaughters, who try to visit their "grandma" at least once a week, together or singly. Sometimes they just talk; sometimes they go out shopping or for lunch.

"All of the residents have physical limitations. They need someone with them to go anywhere," Detato says. Lunches and other events are all Dutch treat; the students and "grandparents" are expected to share their time, not gifts, Detato says.

"When we first introduced the program, the residents were a little wary—they didn't know what we wanted from them. Now the news is out that we want to give to them, and we're getting more people requesting grandchildren," she says.

"Grandma" Guillory thinks the program is wonderful. "All of the girls are equally lovely young ladies, and we're delighted when they visit," she says. "I'm especially impressed that they take time out from their busy schedules to be with us."



Rush College of Nursing student Monica Mastej visits with adopted "grandma" Helen Roche.

A visit to "grandma" provides a welcome time-out, Detato adds: "You get so wrapped up in school, always worrying about the next test or paper. Then you go visit your grandparent. They live such a serene life, and everything is so calm. It helps you keep your sense of perspective."

"Grandma" Rachalle Coletta keeps her granddaughters enthralled with stories about growing up in the 1920s and 30s, especially her experiences in nursing school. "We've got something in common that way, and there are a lot of things that haven't changed," she says.

That makes her a good source of advice for "granddaughter" Wendy Tuzik. "She offers me something I can't learn from a textbook. It seems like she's a lot wiser," Tuzik explains. "My own grandparents have all passed away, so this is a new and valuable experience for me."

The nursing association also sponsors social events for patients in JRB three to four times a month. The program includes trivia games,

as well as bingo and movies, current events discussions and other "thinking activities."

"All SNA members who don't have a grandparent help to plan the social events for patients, and some do both," Detato says. "The patients seem to enjoy it, and the students unanimously agree that it's been fun and educational."

If the Adopt-A-Grandparent program continues to grow, SNA may consider recruiting additional "grandchildren" from the other three colleges in Rush University. "We'd really like this to be a strong, ongoing program," Detato says. "It's good for everyone." K.H.

Study Shows Fish Oil Lowers Cholesterol

Rush researchers are discovering that one way to combat heart disease, a condition affecting 63 million Americans, is with a natural food supplement—fish oil.

Michael Davidson, M.D., instructor, Department of Internal Medi-

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cine and principle investigator of the current studies, explains: "More than 15 years ago, scientist-epidemiologists observed that the Greenland Eskimos had an extremely low incidence of heart disease. They made the correlation between this, the Eskimo's low levels of cholesterol and a diet high in cold water fatty acid fish such as cod, salmon and mackerel."

The oil found in these fish is high in marine omega-3 series of polyunsaturated fats which investigators also discovered retards the formation of platelets and monocytes to the arterial wall, thus preventing atherosclerosis or "hardening of the arteries."

Although marine fish oil capsules have been available in Japan, England and Australia for some time, Dr. Davidson, with Rush scientists John D. Bagdade, M.D., professor, and Papasani Subbaiah, Ph.D., assistant professor, internal medicine, were among the first in the United States to begin studying this cholesterol-lowering substance.

In the first phase, Rush researchers studied 30 patients with elevated cholesterol levels. Fifteen were given a placebo (olive oil), the others, marine oil capsules for 30 days. "We discovered that the marine oil group had a significant reduction in both cholesterol levels and blood pressure, two of the major contributors to heart problems," Dr. Davidson says. "What's remarkable is that these reductions were achieved without change in the patients' diet, lifestyle or behavior."

The precise mechanism by which omega-3 fatty acids lower cholesterol is unknown. Drs. Bagdade and Subbaiah are currently using biochemical analyses to try to explain the process.

Researchers have also embarked on new studies to determine the optimal dose of the fish oil capsules. Dr. Davidson sees use for the capsules with patients who are unable to lower their cholesterol levels with diet only.

"The American diet is low in fish to begin with," he says, "and especially low in omega-3 fatty acid fish. To receive the equivalent of the ingredients in the capsules, a person would have to eat three cans of sardines daily. I don't think many are willing to do this."

The fish oil capsules, which are considered non-prescription drugs, went on the market the first of September. "These capsules have few side effects," Dr. Davidson says. A tendency to prolong bleeding times is one of them. However Dr. Davidson feels there is less potential for problems with the fish oil capsules than with, for example, Vitamin C pills, which, when taken in excess for long periods of time, can cause kidney stones.

"The capsules also have an after-taste much like cod liver oil," he points out. "That should be a deterrent to overuse." M.A.R.

Residency Program Joins Care-Research

Three Rush Medical College graduates recently began a new

residency program which will allow them to continue both their clinical and research interests. Named the Herrick Residency Program after noted Rush physician James B. Herrick, M.D., the program is a two-track, clinical-research residency program for recent medical school graduates who have Ph.D.s.

"One of the concerns in medical schools today is the growing shortage of research-oriented faculty," says Ronald S. Weinstein, M.D., the Harriet Blair Borland professor and chairman of pathology. "Between 80 and 90 percent of medical students with Ph.D.s do not pursue academic careers."

Dr. Weinstein talked with eight graduating Rush Medical College students with Ph.D.s to discover why this is. The students felt the hiatus from their Ph.D. research (often up to eight years) was too long to consider returning to an academic-research career.

To fill this gap between bedside and bench, Dr. Weinstein came up with the idea of a two-track residency program. He shared his idea with Roger Bone, M.D., the Ralph C. Brown, M.D., professor and chair-



Herrick Scholars (front row, from left): Clifford J. Kavinsky, M.D., Ph.D.; Ronald W. McLawhon, M.D., Ph.D.; Patrick Massey,

M.D., Ph.D. Back row, Herrick program organizers: Roger C. Bone, M.D., and Ronald S. Weinstein, M.D.

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man of internal medicine, and together they finalized the concept for the Herrick program.

"We decided to name the residency program after Dr. Herrick, a brilliant clinician who combined clinical experience with basic science and is the perfect role model for future academicians," Dr. Weinstein says. Dr. Herrick was the first to define sickle cell anemia and coronary heart disease, and, with colleague Fred Smith, M.D., to describe coronary occlusion on an EKG. He was a founding member and the first president of the Illinois Medical Society.

Like Dr. Herrick, this year's Herrick residents will combine their clinical experience with research.

Two are working in the Department of Medicine, one in the Department of Pathology. Patrick Massey, M.D., Ph.D., will develop a project in pulmonary medicine. Dr. Massey received his Ph.D. from the Northwestern University Medical School. During his medical training he received the Northwestern University Research Fellowship, Nellie Fox Fellowship and the Rush University scholarship.

Clifford J. Kavinsky, M.D., Ph.D., will be pursuing research in oncology and infectious disease. He received his Ph.D. in biology from The University of Chicago, combining work in biochemistry, immunology and cell biology.

Ronald W. McLawhon, M.D., Ph.D., received his Ph.D. in biochemistry from The University of Chicago and is an expert on cell surface receptors. Dr. McLawhon already has over 20 publications to his credit. He will do research in the Department of Pathology on the actions of prostaglandins and in the area of in situ hybridization.

Criteria for acceptance into the residency program include a commitment to an academic career and approval of the chairman of the department in which they wish to work.

"During the first year, the residents develop research protocols.

The second and third years are spent working on the project," explains Dr. Bone. "Time is built into the curricula in the second and third years to allow blocks of time for concentrated research. Residents receive a stipend from the department in which they are working."

Herrick residents enter the program with the faculty designation of instructor but by the second year are eligible for the rank of assistant professor.

Both Drs. Weinstein and Bone feel that the Herrick Residency Program puts Rush in a competitive position to attract outstanding physician-researchers. "To my knowledge, this is the only program of its kind in the country," Dr. Weinstein says. "I believe it will help fill the need for academicians in medical schools."

Three-quarters of a century ago, Dr. Herrick said that "unless the spirit of research is in the hospital...the educational function of the hospital languishes...things fail to progress and the patients suffer." Dr. Weinstein echoes these thoughts when he observes that the Herrick Residency Program will also nurture the concept of the physician-scientist, who is proving to be essential to providing quality patient care.

M.A.R.

Harvey Named Head of Rehabilitation

Richard F. Harvey, M.D., has been named professor and chairman of the Department of Physical Medicine and Rehabilitation at Rush-Presbyterian-St. Luke's Medical Center.

Dr. Harvey comes to the Medical Center from Marianjoy Rehabilitation Center, Wheaton, Illinois, where, since 1982, he has been and continues to serve as vice president, chief medical officer and physiatrist. He will also remain as president of the Rehabilitation Medicine Clinic of DuPage Service



Richard F. Harvey, M.D.

Corporation, Wheaton.

Dr. Harvey organized and chaired the first department of rehabilitation medicine at the University of Wisconsin-Madison Medical School. Prior to his appointment at Wisconsin he was associate professor, physical medicine and rehabilitation, Rockford School of Medicine, University of Illinois, and director and vice president for medical affairs at the Rockford Memorial Hospital Van Matre Rehabilitation Center.

Dr. Harvey is a member of several professional organizations, an academy editorial board member and manuscript reviewer for the *Archives of Physical Medicine and Rehabilitation*, and the *Journal of the American Medical Association*. His research studies have focused on multiple areas of physical rehabilitation.

A Rockford native, Dr. Harvey earned his B.A. degree at Augustana College, Rock Island, Illinois, and his M.D. degree at the University of Illinois College of Medicine, Chicago. He completed his residency and fellowship in physical medicine and rehabilitation at the Mayo Clinic in Rochester, Minnesota. He has published and presented numerous papers and, in 1981, was invited to become a member of the United States' special rehabilitation medicine delegation to the Peoples' Republic of China.

J.F.

Study Focuses on Radiation Protection

A three-year \$400,000 contract from the Defense Nuclear Agency of the federal government has been awarded to Rush investigator Wayne R. Hanson, Ph.D., associate scientist and director of the radiobiology section of therapeutic radiology, to study compounds which could protect humans from dangerous doses of radiation.

The compounds under study by Dr. Hanson are known as prostaglandins, which are produced by many cells of the body. Specifically, Dr. Hanson is looking at how combinations of different types of synthetic and natural prostaglandins, when combined with a sulfhydryl drug known as WR-2721, react to protect cells against the toxic effects of radiation.

"We've made enough progress thus far to know that some prostaglandins with a different structure are showing more protection against radiation than the ones we knew about previously," said Dr. Hanson. The big problem facing Dr. Hanson and his research team is the toxicity of WR-2721. At present, Dr. Hanson is injecting laboratory mice, exposed to various kinds of radiation, with WR-2721. The two compounds—prostaglandins and WR-2721—appear to have an additive effect when given together. An ongoing task is to determine which prostaglandins are most effective when given alone or in combination with WR-2721 and what mechanisms make them work together.

WR-2721's toxic effect also limits its usefulness in protecting normal tissue in cancer treatment, according to Dr. Hanson. "It would be advantageous to have a radioprotective agent or combination of agents which could reach normal tissue but not reach tumors. Then we could increase the radiation dose to tumors without increasing the damage to normal tissue."

The various combinations tried

could reduce some of the acute effects of radiation, but their effect on long-term problems such as cancer is still unknown.

However, the prostaglandin research may improve cancer treatment. "Tumors produce many prostaglandins, which may decrease the effectiveness of radiation therapy," noted Dr. Hanson, "We're trying to use agents to block prostaglandin production to see if tumor tissue is easier to destroy."

Dr. Hanson hopes that by using a lower dose of the toxic sulfhydryl drugs in combination with prostaglandins or their chemical cousins it will be possible to protect humans against radiation without producing undesirable drug side effects.

The research Dr. Hanson is spearheading also utilizes the facilities at Argonne National Laboratory, Argonne, Illinois, and at Fermi National Accelerator Laboratory in Batavia, Illinois.

C.E.

Rush People Honored

• "Innovation, leadership, vision and exceptional organizational abilities." These were some of the qualities American Hospital Publishing, Inc., was looking for when deciding who were the health care industry's top 50 young professionals of the year. Only one candidate was selected from each state, and representing Illinois is Wayne M. Lerner, M.H.A., vice president, administrative affairs, at the Medical Center. Lerner was profiled in *Hospitals* magazine in May.

• Last summer Sharon Bartels, R.N., surgical nursing, was strolling around the White Lake Shopping Center in Topeka, Kansas, when a male shopper went into cardiac arrest. Immediately Bartels went to his aid and administered CPR. Another passerby came to help out, and the man was taken to a hospital. He survived. The other passerby, a member of the American Legion, notified that



Rush Medical College student Dipali Apte, first prize winner in the 1986 Secretary's Award competition, and James A. Schoenberger, M.D., chairman, Department of Preventive Medicine.

organization about the incident. The result: the American Legion awarded a certificate of thanks to Bartels.

• Ruth G. Ramsey, M.D., professor of radiology at the Medical Center, is the first woman to head the 73-year-old Chicago Radiological Society. She assumed the presidency of the 700-member society following a two-year term as secretary-treasurer.

• Dipali V. Apte, a second-year Rush Medical College student, won first prize in the fourth annual Secretary's Award for Innovations in Health Promotion and Disease Prevention, a nationwide competition for health professions students. Health and Human Services Secretary Otis R. Bowen, M.D., presented a plaque and a \$3,000 prize to Apte in July, 1986, at a ceremony in Washington, D.C. Apte's proposal, a three-part program to prevent adolescent pregnancy through sex education, clinical care and community support, will be published in *Public Health Reports*.

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New Study Reveals Why Nurses Burn Out

An open secret among medical care professionals—and often the theme of hospital TV shows—is nurse burnout. When it strikes, even the most attentive nurse suffers total exhaustion and suddenly loses compassion for her patients. The cause of burnout has almost always been thought to be stress, the response of the being to demands placed on it. However, results of a unique study of nearly 300 nurses at three medical centers now indicate that stress is but one of the factors.

One of the surprises of the study is the finding that nurses who care for patients under relatively minor stress conditions burn out more frequently than do nurses who work under relatively high-stress conditions.

According to Diane Cronin-Stubbs, Ph.D., R.N., who conducted the study, "Stress does not equal burnout. In fact, stress represents only about 37 percent of the factors involved." Dr. Cronin-Stubbs, who is assistant chair and graduate program coordinator in the Department of Psychiatric Nursing at Rush-Presbyterian-St. Luke's Medical Center, identified burnout as "spiritual and physiological fatigue, not just emotional fatigue. All your energy is tapped."

Her study was conducted among 296 female, full-time staff nurses chosen at random from three large metropolitan medical centers (900 to 1100 beds each). The nurses worked in one of four specialty areas: medicine, psychiatry, surgery, and intensive care. Typically, the women were single, 21-to-30 years old, had bachelor's degrees, and had been in primary care nursing for between two and ten years.

All the nurses who were studied completed questionnaires; many were also selected, on a random basis, for personal interviews. "Results of the interviews," re-

ported Dr. Cronin-Stubbs, "indicated that differences existed not only in the nursing tasks performed, but also in the estimated amounts of interpersonal involvement and conflict experienced by the nurses."

Specifically psychiatric nurses had intense involvement and frequent conflicts with patients, families, colleagues and doctors;—operating room nurses had little involvement with patients, families or colleagues but frequent conflicts with doctors;—intensive care and medical nurses had only moderate interaction with patients and occasional conflicts with families, colleagues and doctors.

Among the four specialists, psychiatric and operating room nurses most frequently experienced burnout.

Ironically, between the two, psychiatric nurses more frequently burn out than operating room nurses. The reason, said Dr. Cronin-Stubbs, is that most of the psychiatric nurses' care occurs as interactions with patients. "There is no friend or colleague to talk to and get feedback from. At home, they find it difficult to step out of their roles as helpers and to engage in mutually validating relationships. On the other hand, operating room nurses are part of a team who depend on each other for support, so they are more experienced, at work and at home, in seeking help from others."

Even so, the stress of caring for very sick, even dying patients is not the only precipitant to burnout. Personal factors are critical also. In nurses who burn out, the Rush researcher found, occupational stress is a partner to personal stress. "Nurses seldom get a chance to deal with their own feelings," she explained. "They don't know how to ask for help—or even whom to ask. They rely on themselves alone and ask too much of themselves. They just go from work to home to work. Some rely on calming drugs. It's too much and sooner or later some-

thing triggers the burnout. They become totally exhausted and unable to work. They are burned out."

She added, "In the critical care setting, the death of one patient may affect nurses more adversely than the pressures of caring for acutely ill patients." This indicates that the repetitiveness of job stress doesn't contribute as much to burnout as does the perceived impact, or the intensity, of stress.

The results of her study have helped Dr. Cronin-Stubbs construct some guidelines to help nurses prevent burnout. Nurses have to learn to be assertive and to negotiate so they can set limits in their jobs and be able to ask for help. Also, "teams that serve chronically ill and severely ill patients can be rotated with teams which serve acutely ill patients."

But most importantly, nurses need to take a look around and see what kind of personal support systems they have. Key elements in such a system are long-term relationships rather than frequently being in contact with members of the social network. Each needs a friend or colleague or spouse—or all three—to turn to for help, to talk to, to get affirmation from.

"To prevent burnout," she advises other nurses, "We need to take care of ourselves." T.B.

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